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* * * * * * * * * * *   Welcome to STN International   * * * * * * * * * * *
* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

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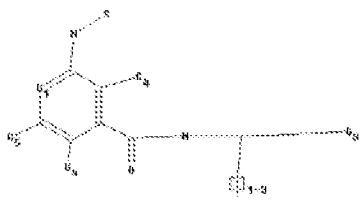

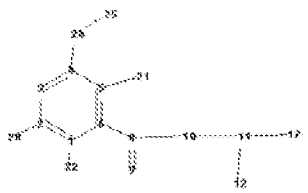

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8  9  10  11  12  14  17  19  21  22  24  25  28
ring nodes :
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ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
1-2  1-6  1-22  2-3  2-28  3-4  4-5  4-24  5-6  5-21  6-8  8-9  8-10  10-11  11-17
11-12  12-14  17-19  24-25
isolated ring systems :
containing 1 :


G1:CH,N

G2:Cy,Ak

G3:OH,NH2

G4:H,X

G5:C,O,S,N

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  8:CLASS  9:CLASS  10:CLASS
11:CLASS  12:CLASS  14:CLASS  17:CLASS  19:CLASS  21:CLASS  22:CLASS  24:CLASS
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=> dis l5 1-5 bib abs hitstr

L5   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2007 ACS on STN
AN   2003:696859  CAPLUS  Full-text
DN   139:230480
TI   Preparation of substituted amines prodrugs useful in treating Alzheimer's
     disease
IN   Varghese, John; Jagodzinska, Barbara; Maillard, Michel; Beck, James P.;
     Tenbrink, Ruth E.; Getman, Daniel
PA   Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn
SO   PCT Int. Appl., 483 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     MX 2004PA08317       A     20050608    MX 2004-PA8317         20040826
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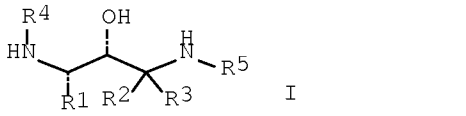

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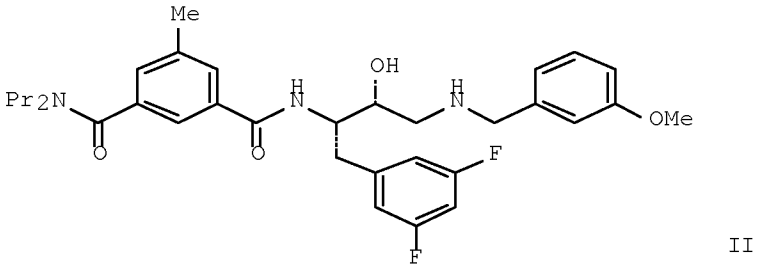


II

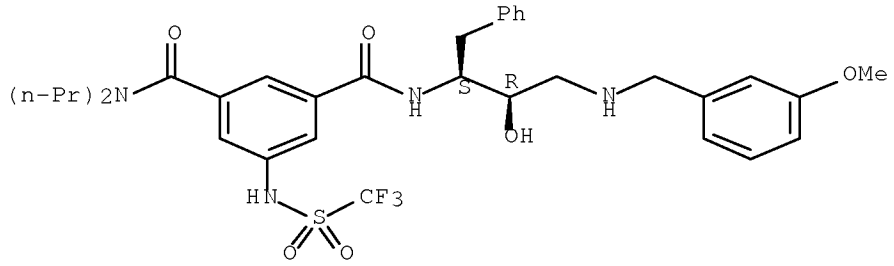
AB Amines [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO2, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH2)0-3cycloalkyl, etc.; e.g. N1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3- methoxybenzyl)amino]propyl]-5-methyl-N3,N3-dipropylisophthalamide], useful in treating Alzheimer's disease and other similar diseases, were prepared Although the methods of preparation are not claimed, hundreds of example prepns. are included. Thus, reacting (2R,3S)-3-amino-4-(3,5- difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamic acid in the presence of Et3N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II (N1-[(1S,2R)-1-(3,5- difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N3,N3- dipropylisophthalamide). The compds. I exhibit an IC50 of < 50 μM against β-secretase.

IT 388066-53-3P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N',N'-dipropyl-5-[[(trifluoromethyl)sulfonyl]amino]isophthalamide 388066-61-3P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-[(phenylsulfonyl)amino]-N',N'-dipropylisophthalamide 388066-71-5P, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl]-N',N'-dipropyl-5-[[(trifluoromethyl)sulfonyl]amino]isophthalamide 388072-06-8P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-[(methylsulfonyl)amino]-N',N'-dipropylisophthalamide hydrochloride 388072-07-9P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N',N'-dipropyl-5-[[(thien-2-yl)sulfonyl]amino]isophthalamide hydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of substituted amine prodrugs useful in treating Alzheimer's disease)

RN 388066-53-3 CAPLUS

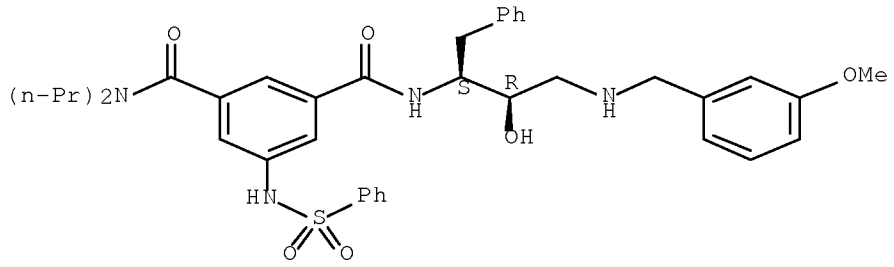
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl-5-[[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



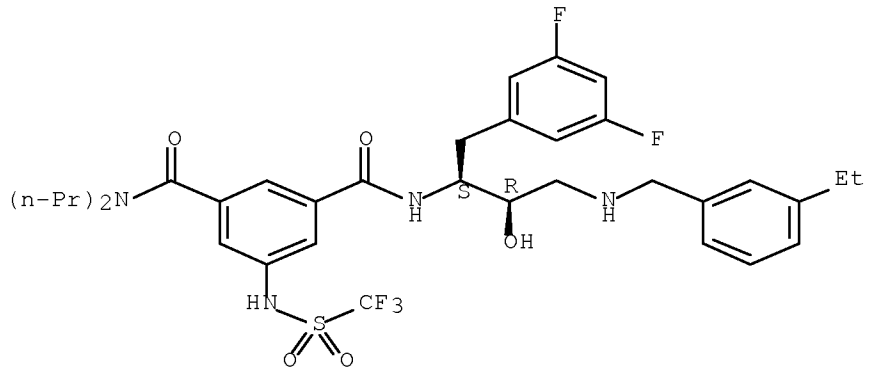
RN 388066-61-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-[(phenylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



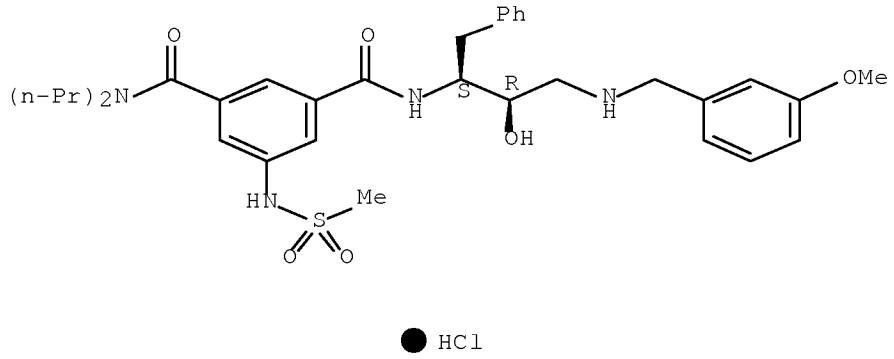
RN 388066-71-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-N,N-dipropyl-5-[[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388072-06-8 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-[(methylsulfonyl)amino]-N,N-dipropyl-, monohydrochloride (9CI) (CA INDEX NAME)

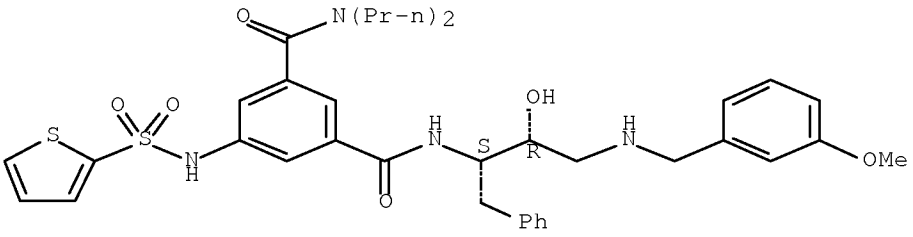
Absolute stereochemistry.



● HCl

RN 388072-07-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl-5-[(2-thienylsulfonyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:412801 CAPLUS Full-text
DN 139:245782
TI Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease
IN Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy
PA Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SO PCT Int. Appl., 1243 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

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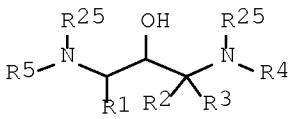

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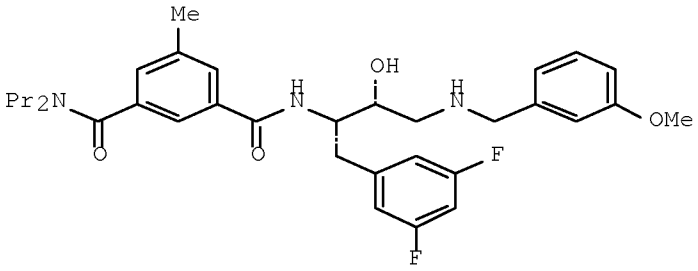


II

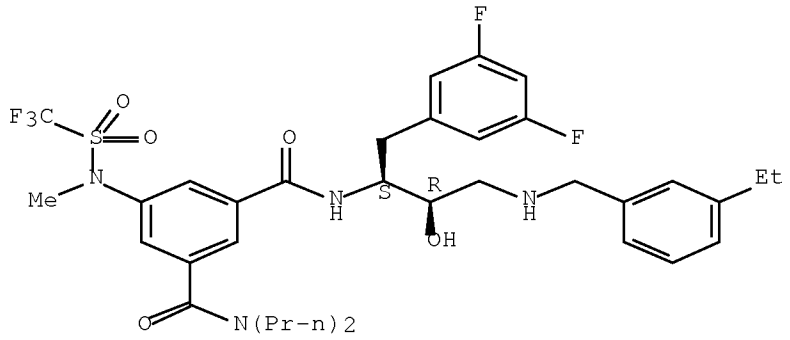
AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO2, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO2, (un)substituted CH2; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of β-secretase and are therefore useful in treating a variety of

disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC50 of < 20 μM in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 2 of 1-2 series.

IT 388068-39-1P 388070-61-9P 388070-97-1P
527726-99-4P 527727-34-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

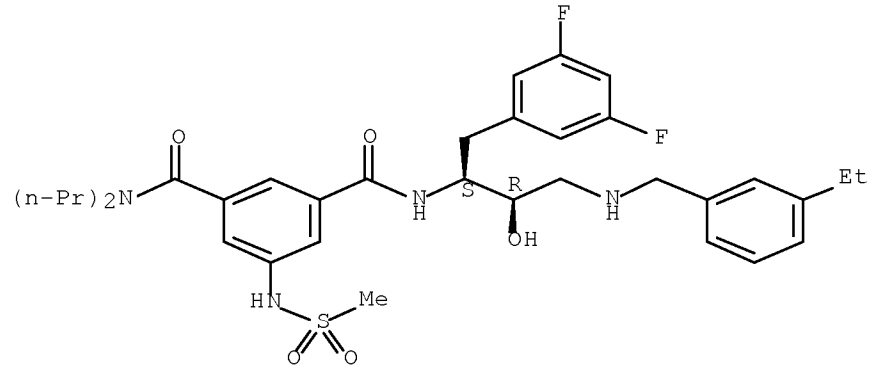
RN 388068-39-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[methyl[(trifluoromethyl)sulfonyl]amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388070-61-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388070-97-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-

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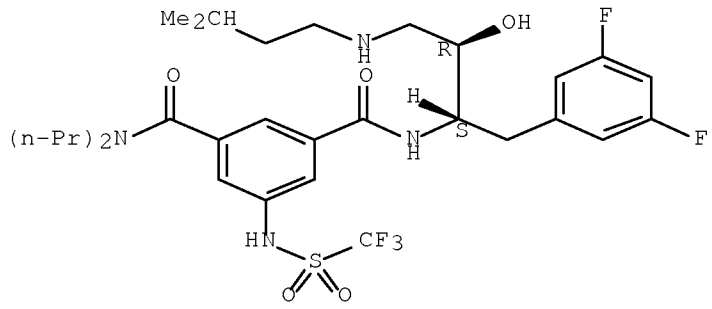
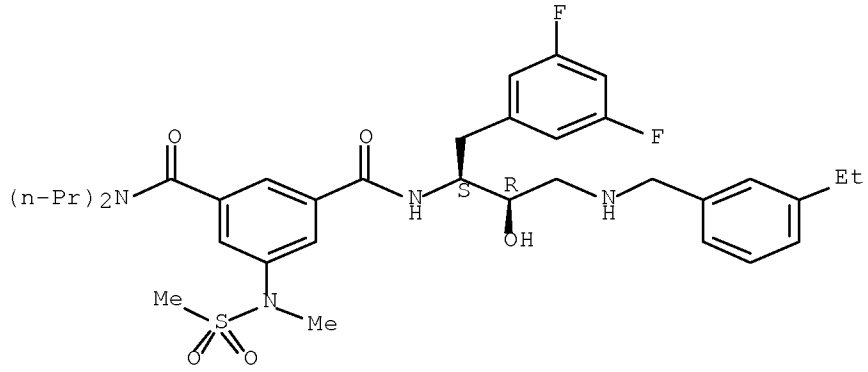
Absolute stereochemistry.



RN 527726-99-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[methyl(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

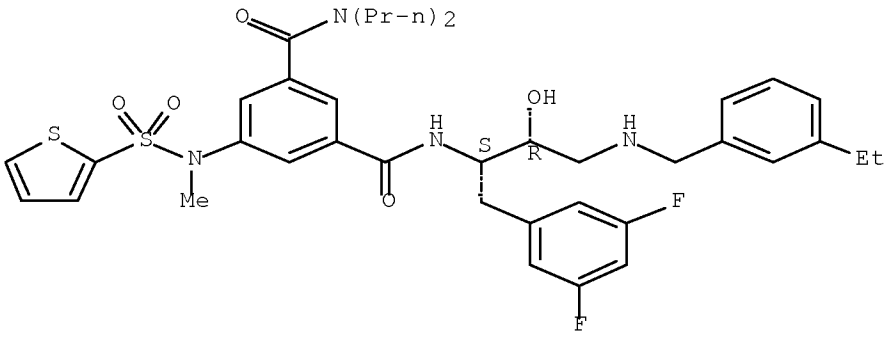
Absolute stereochemistry.



RN 527727-34-0 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[methyl(2-thienylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:376819 CAPLUS Full-text
DN 138:385173
TI Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease
IN Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy
PA Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SO PCT Int. Appl., 1243 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

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US 7176242	B2	20070213		
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

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	US 2001-344086P	P	20011228		
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OS MARPAT 138:385173

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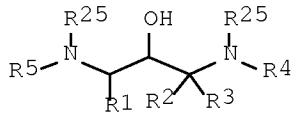

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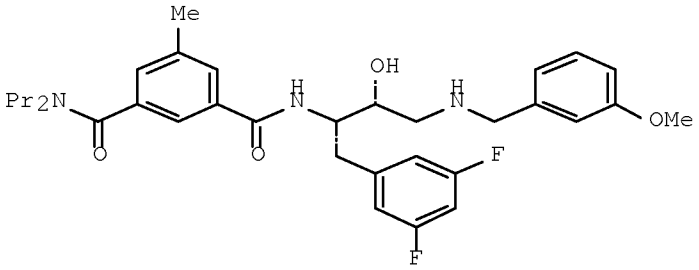


II

AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO2, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO2, (un)substituted CH2; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of β-secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC50 of < 20 μM in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 1 of 1-2 series.

IT 388068-39-1P 388070-61-9P 388070-97-1P
388071-00-9P 527726-99-4P 527727-34-0P

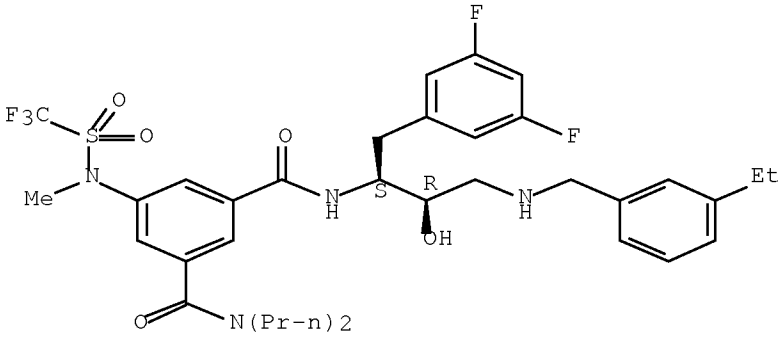
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 388068-39-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[methyl[(trifluoromethyl)sulfonyl]amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

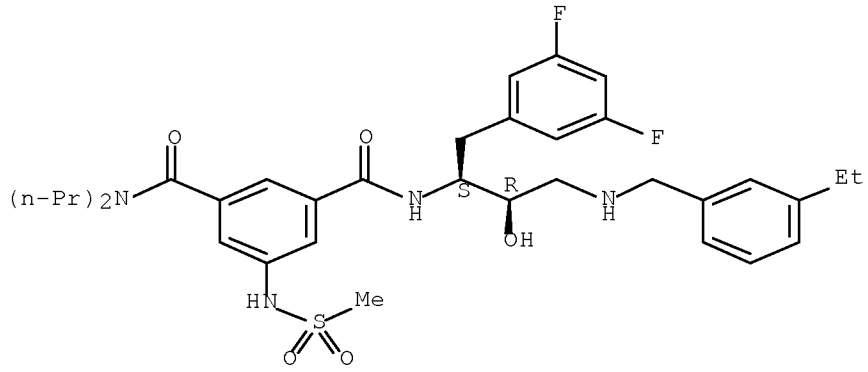
Absolute stereochemistry.



RN 388070-61-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

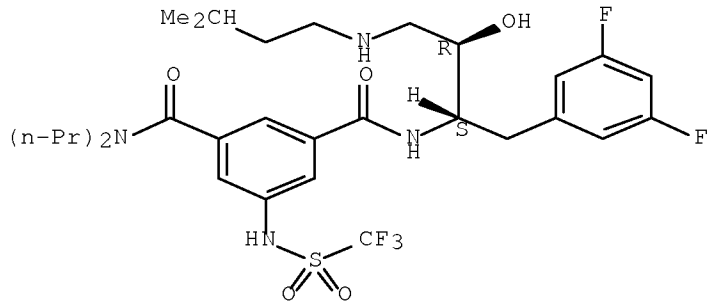
Absolute stereochemistry.



RN 388070-97-1 CAPLUS

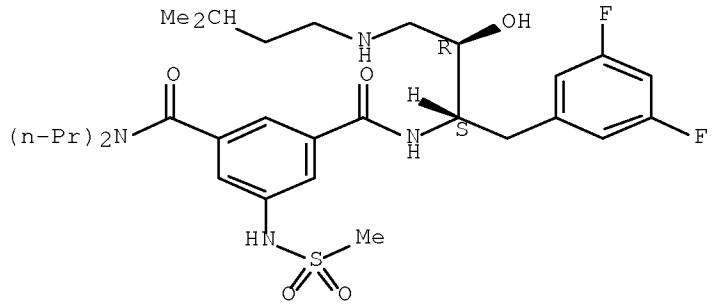
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(3-methylbutyl)amino]propyl]-N,N-dipropyl-5-[[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



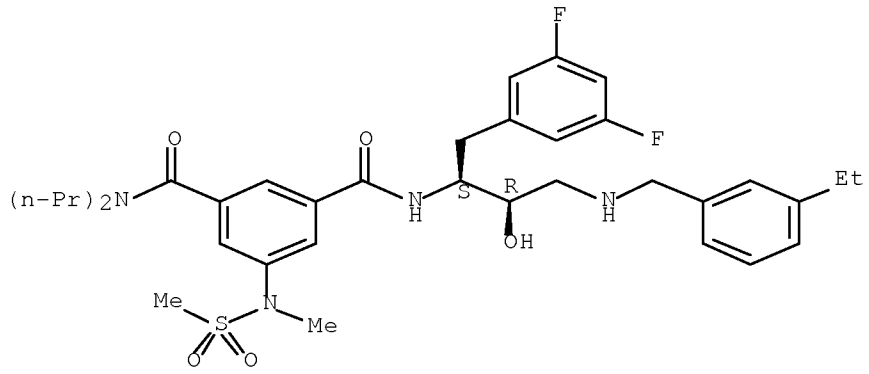
RN 388071-00-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(3-methylbutyl)amino]propyl]-5-[(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 527726-99-4 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[methyl(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

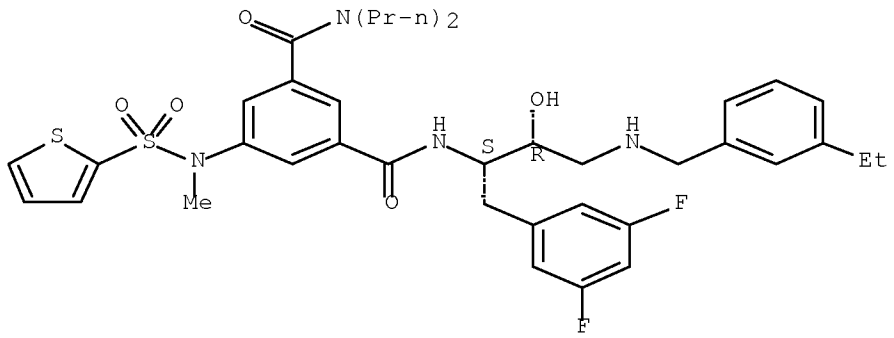
Absolute stereochemistry.



RN 527727-34-0 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[methyl(2-

thienylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:31402 CAPLUS Full-text
DN 136:102190
TI Preparation of substituted amines to treat Alzheimer's disease
IN Maillaird, Michel; Hom, Court; Gailunas, Andrea; Jagodzinska, Barbara; Fang, Lawrence Y.; John, Varghese; Freskos, John N.; Pulley, Shon R.; Beck, James P.; Tenbrink, Ruth E.
PA Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SO PCT Int. Appl., 651 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EE 200200716	A	20040816	EE 2002-716	20010629
NZ 522899	A	20050624	NZ 2001-522899	20010629
EP 1586556	A2	20051019	EP 2005-8935	20010629

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	US 2007213407	A1	20070913	US 2006-529749	20060928	
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	EP 2001-952352	A3	20010629			
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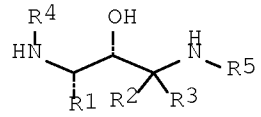
OS MARPAT 136:102190

GI



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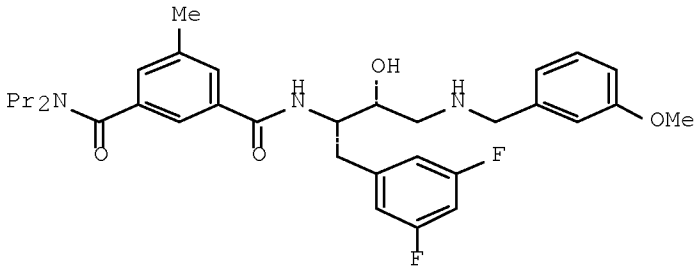

II

AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO2, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH2)0-3cycloalkyl, etc.], useful in treating Alzheimer's disease and other similar diseases, were prepared Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3- methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N- dipropylisophthalamic acid in the presence of Et3N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II. The compds. I exhibit an IC50 of < 50 μM against beta-secretase.

IT 388066-53-3P 388066-56-6P 388066-57-7P

388066-61-3P 388066-71-5P 388068-37-9P
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388070-67-5P 388070-68-6P 388070-69-7P
388070-70-0P 388070-71-1P 388070-72-2P
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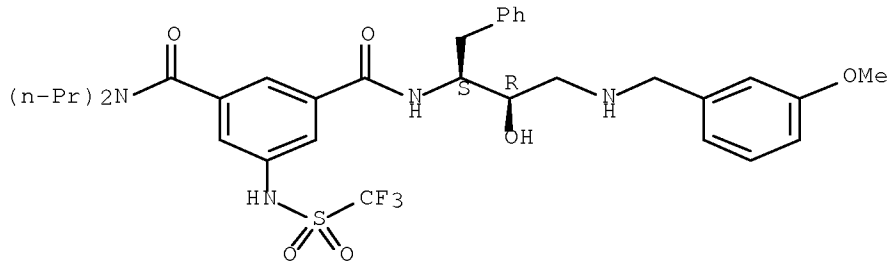
388071-00-9P 388072-06-8P 388072-07-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted amines for treating Alzheimer's disease)

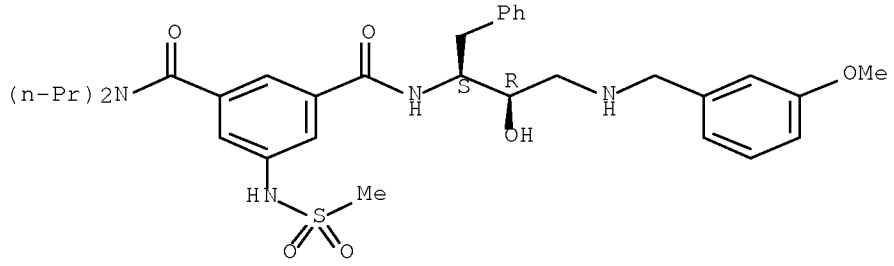
RN 388066-53-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl-5-[[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



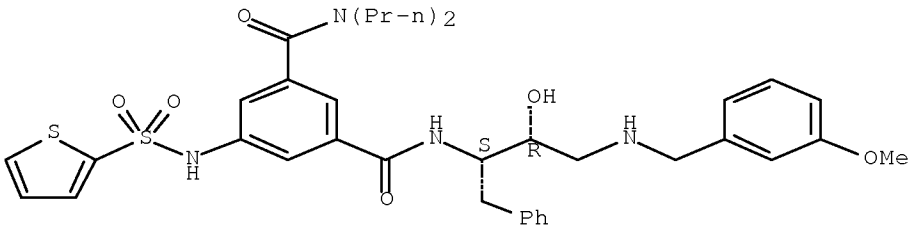
RN 388066-56-6 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-[(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



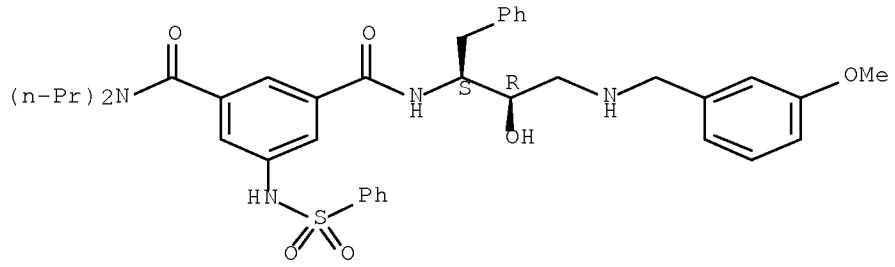
RN 388066-57-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl-5-[(2-thienylsulfonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



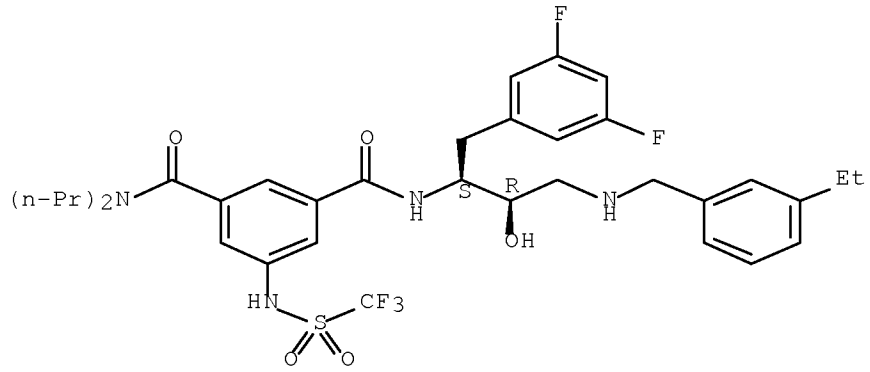
RN 388066-61-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-[(phenylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



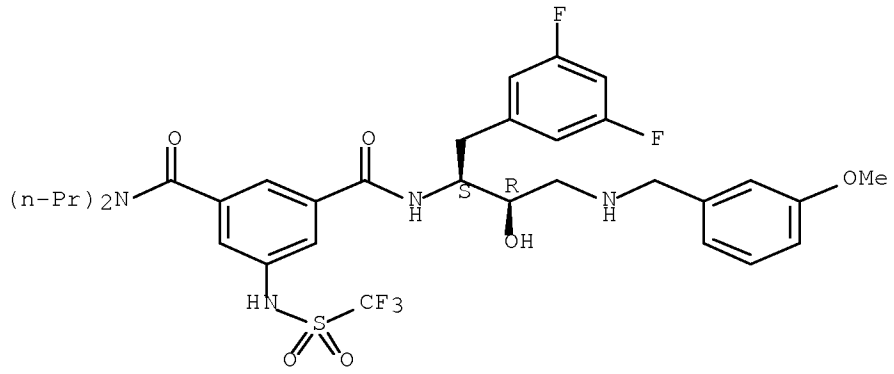
RN 388066-71-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-N,N-dipropyl-5-[[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388068-37-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]propyl]-N,N-dipropyl-5-[[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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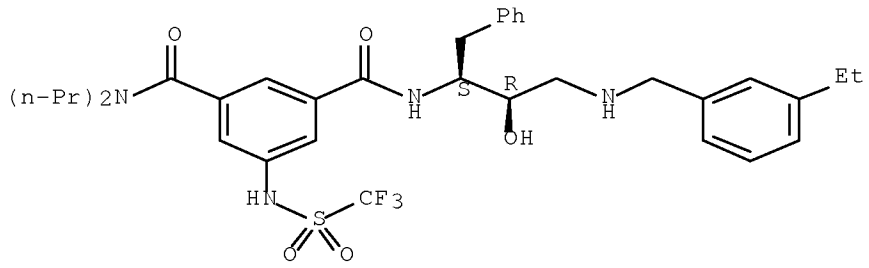
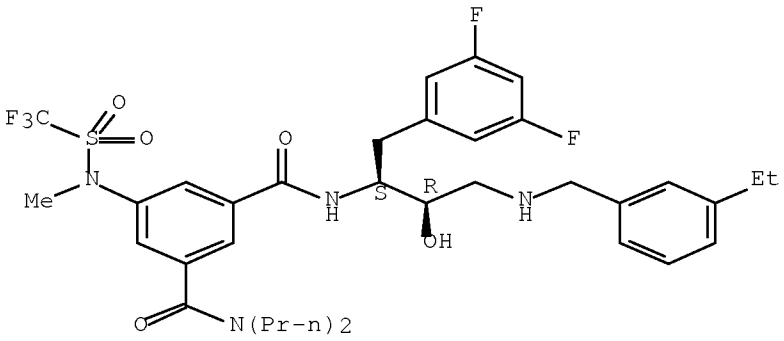
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl-5-[[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388068-39-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[methyl[(trifluoromethyl)sulfonyl]amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

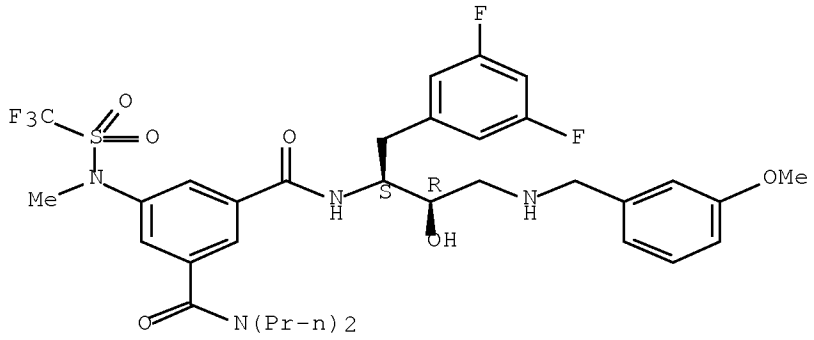
Absolute stereochemistry.



RN 388068-40-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]propyl]-5-[methyl[(trifluoromethyl)sulfonyl]amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

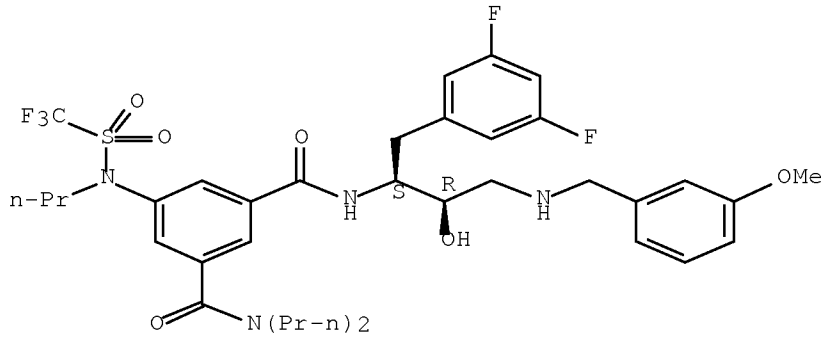
Absolute stereochemistry.



RN 388068-41-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]propyl]-N,N-dipropyl-5-[propyl[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

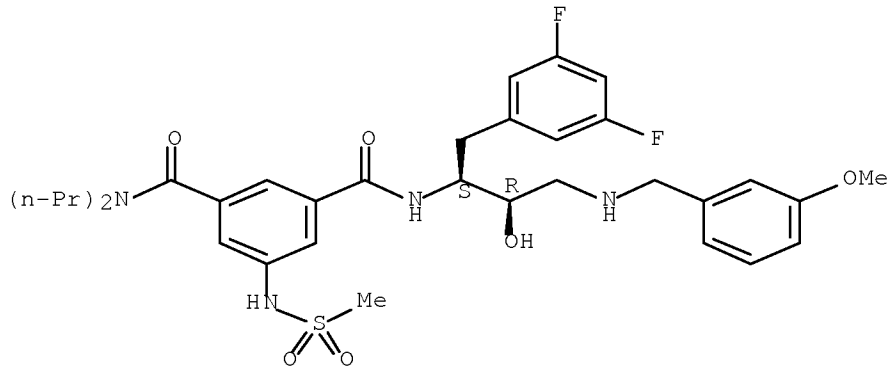
Absolute stereochemistry.



RN 388068-42-6 CAPLUS

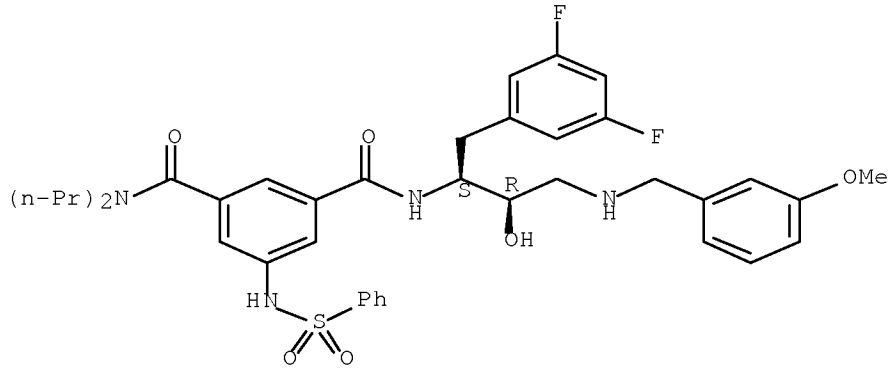
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]propyl]-5-[(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



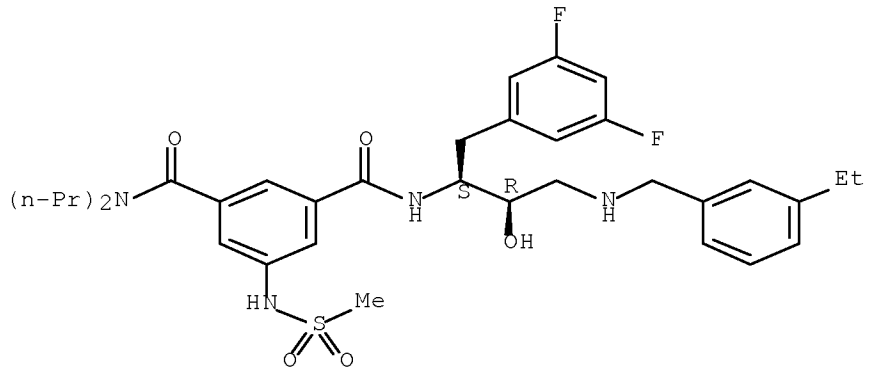
RN 388068-43-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]propyl]-5-[(phenylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



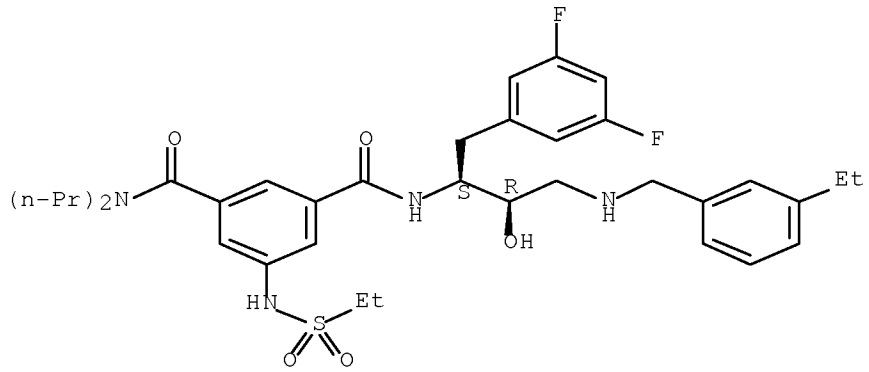
RN 388070-61-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



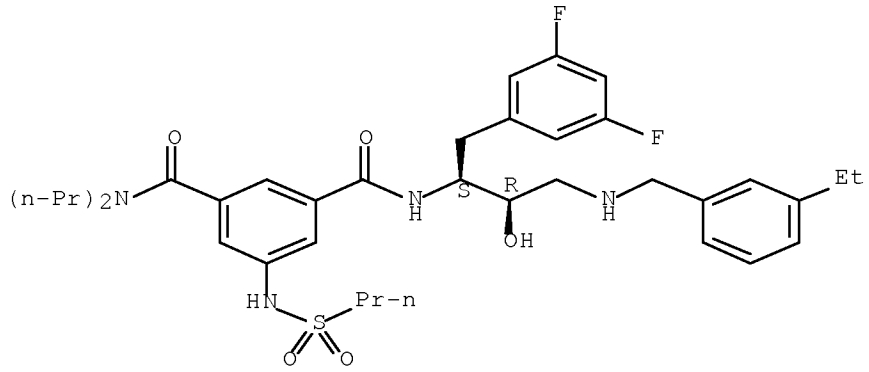
RN 388070-62-0 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[(ethylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



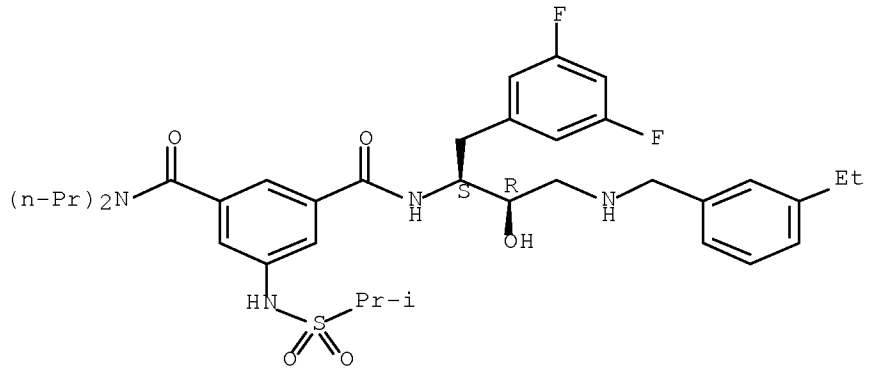
RN 388070-63-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-N,N-dipropyl-5-[(propylsulfonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



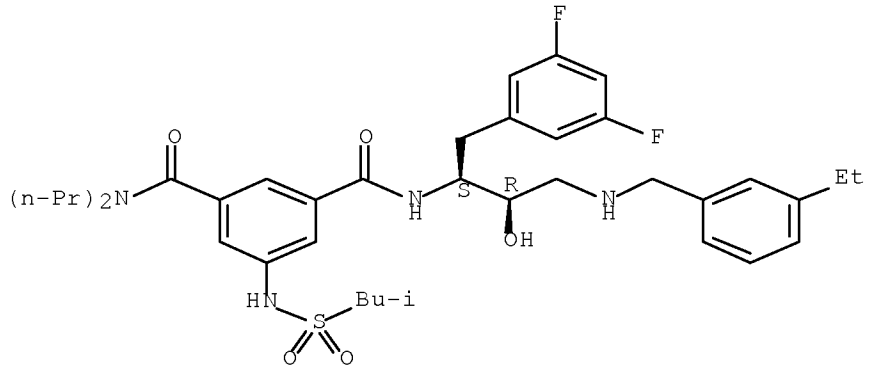
RN 388070-64-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[[(1-methylethyl)sulfonyl]amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



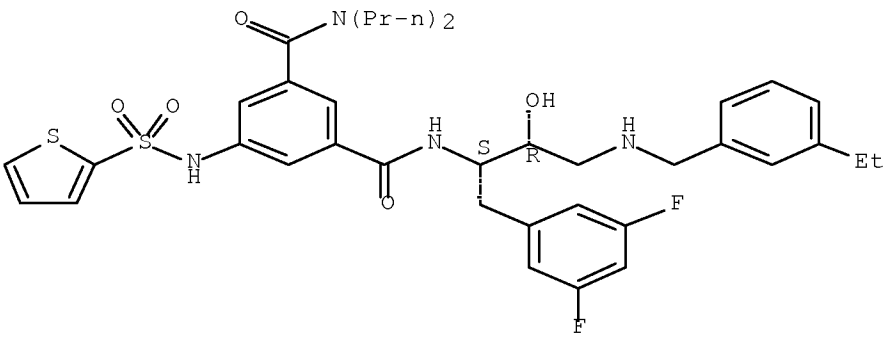
RN 388070-65-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[[(2-methylpropyl)sulfonyl]amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



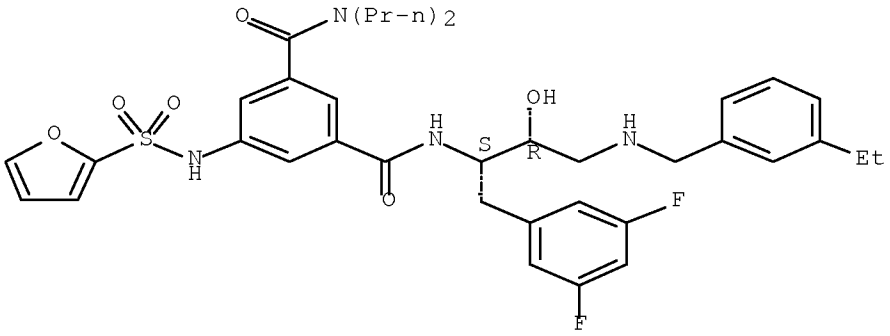
RN 388070-66-4 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-N,N-dipropyl-5-[(2-thienylsulfonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



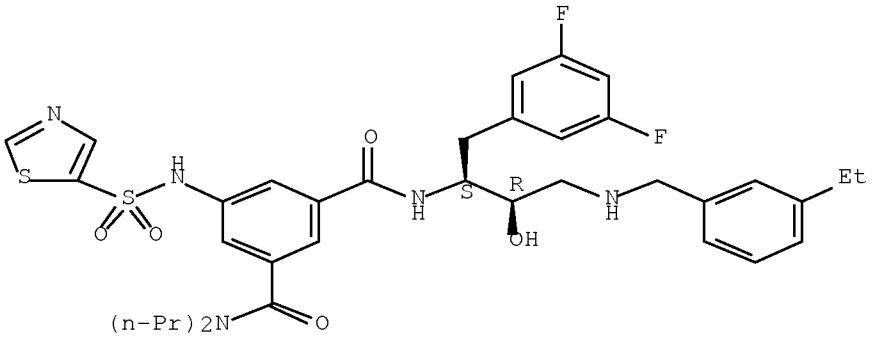
RN 388070-67-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[(2-furanylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



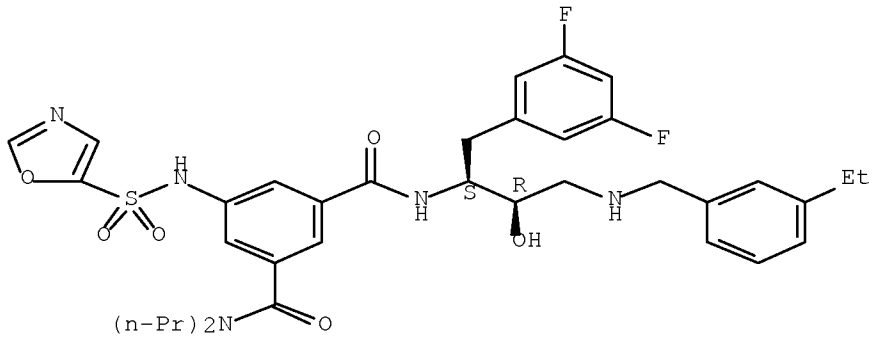
RN 388070-68-6 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-N,N-dipropyl-5-[(5-thiazolylsulfonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



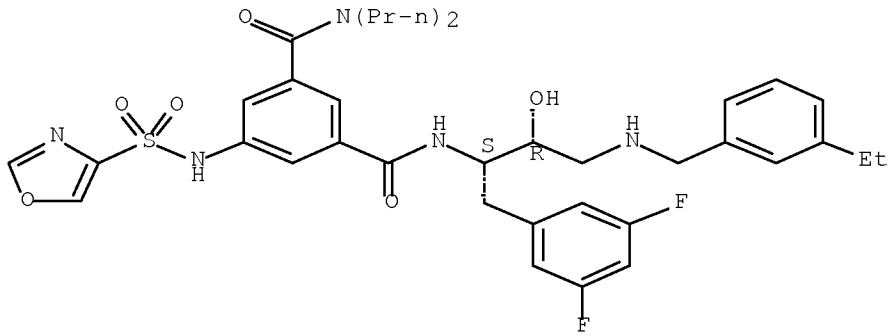
RN 388070-69-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[(5-oxazolylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



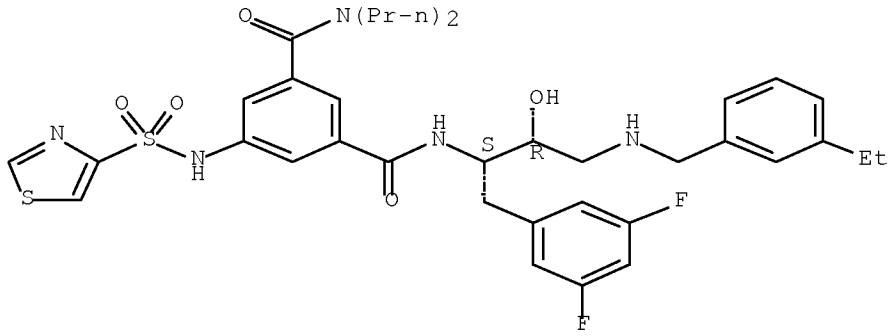
RN 388070-70-0 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[(4-oxazolylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388070-71-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-N,N-dipropyl-5-[(4-thiazolylsulfonyl)amino]- (9CI) (CA INDEX NAME)

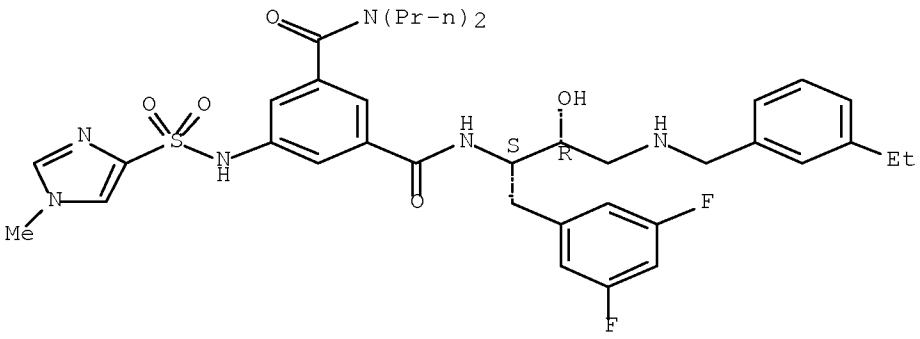
Absolute stereochemistry.



RN 388070-72-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-

[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

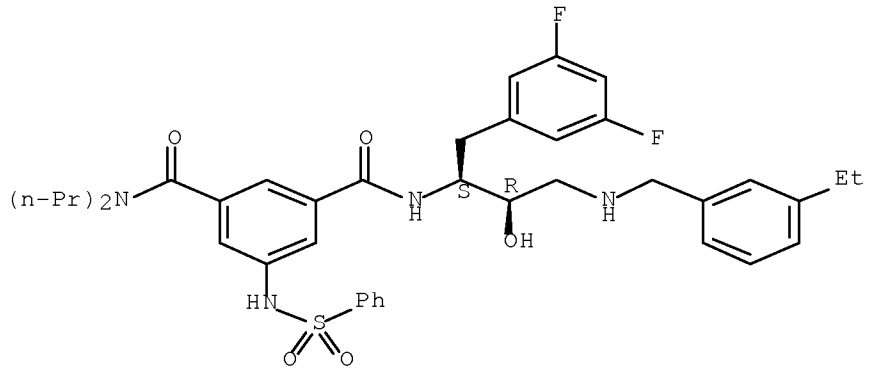
Absolute stereochemistry.



RN 388070-73-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[(phenylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

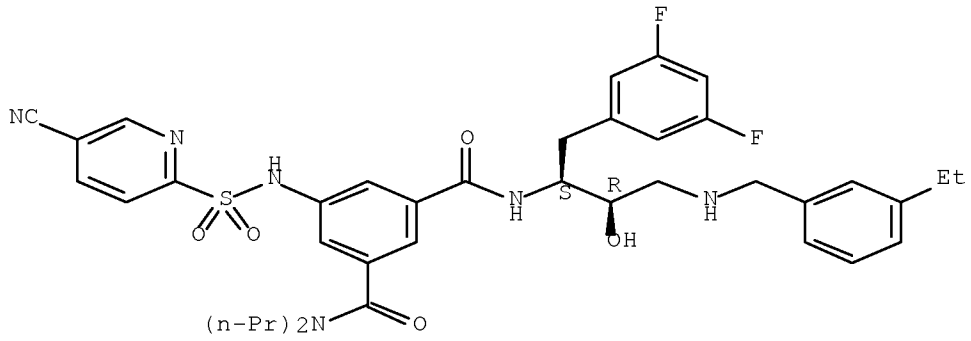
Absolute stereochemistry.



RN 388070-74-4 CAPLUS

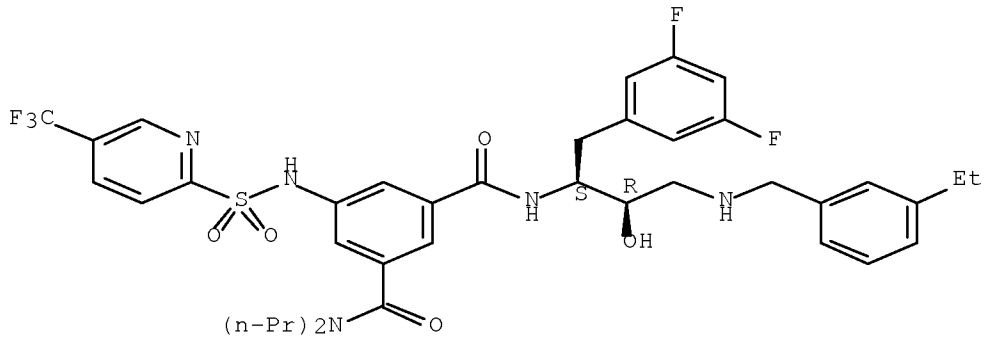
CN 1,3-Benzenedicarboxamide, 5-[[(5-cyano-2-pyridinyl)sulfonyl]amino]-N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



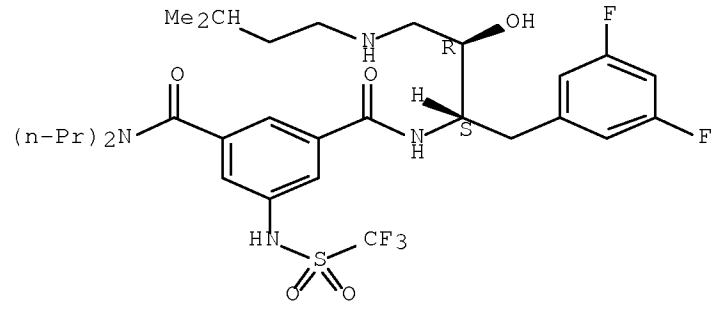
RN 388070-75-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-N,N-dipropyl-5-[[[5-(trifluoromethyl)-2-pyridinyl]sulfonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388070-97-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(3-methylbutyl)amino]propyl]-N,N-dipropyl-5-[[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

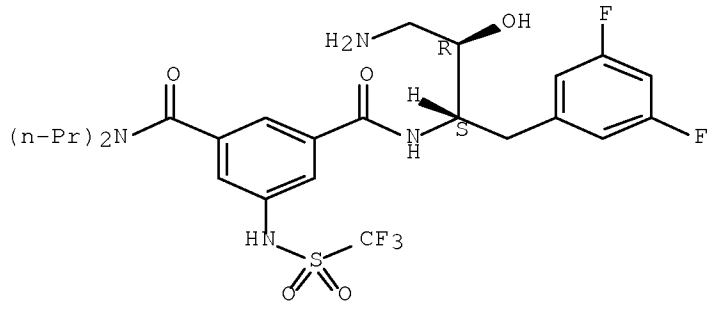
Absolute stereochemistry.



RN 388070-98-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-amino-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-N,N-dipropyl-5-

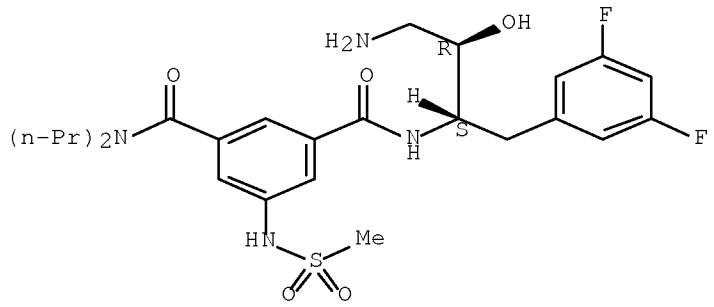
[[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



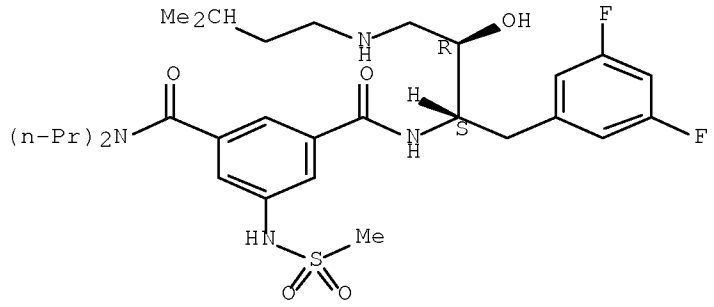
RN 388070-99-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-amino-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-5-[(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388071-00-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(3-methylbutyl)amino]propyl]-5-[(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

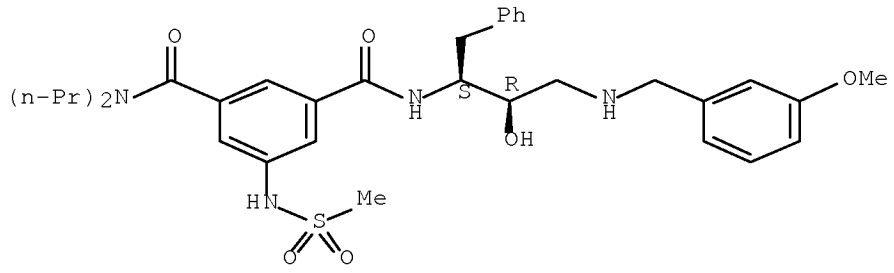
Absolute stereochemistry.



RN 388072-06-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-[(methylsulfonyl)amino]-N,N-dipropyl-, monohydrochloride (9CI) (CA INDEX NAME)

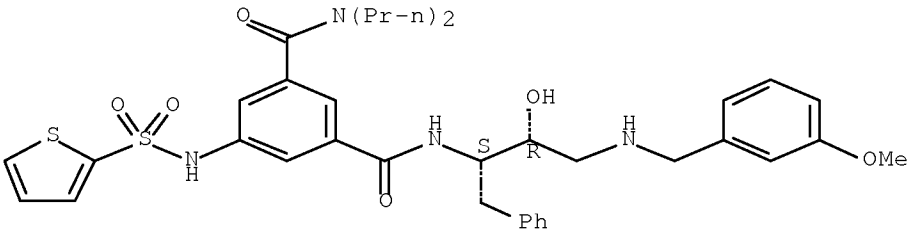
Absolute stereochemistry.



● HCl

RN 388072-07-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl-5-[(2-thienylsulfonyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:686832 CAPLUS Full-text
DN 131:286267
TI Preparation of phthalic acid monoamides as calpain and cathepsin inhibitors
IN Lubisch, Wilfried; Moeller, Achim; Treiber, Hans-Joerg; Knopp, Monika
PA BASF A.-G., Germany
SO Ger. Offen., 14 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19818614	A1	19991021	DE 1998-19818614	19980420 <--

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     CA 2328435          A1    19991028    CA 1999-2328435        19990419 <--
     WO 9954294          A1    19991028    WO 1999-EP2618         19990419 <--
         W:  AL, AU, BG, BR, BY, CA, CN, CZ, GE, HR, HU, ID, IL, IN, JP, KR,
             KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US,
             ZA, AM, AZ, KG, MD, TJ, TM
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     AU 9936071          A     19991108    AU 1999-36071          19990419 <--
     AU 753402           B2    20021017
     BR 9909775          A     20001219    BR 1999-9775           19990419 <--
     TR 200003028        T2    20010122    TR 2000-3028           19990419 <--
     EP 1073631          A1    20010207    EP 1999-917996         19990419 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
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     HU 2001001624       A2    20011128    HU 2001-1624           19990419 <--
     HU 2001001624       A3    20030228
     JP 2002512221       T     20020423    JP 2000-544635         19990419 <--
     US 6448254          B1    20020910    US 2000-647677         20001003 <--
     MX 2000PA09755      A     20010316    MX 2000-PA9755         20001005 <--
     BG 104855           A     20010531    BG 2000-104855         20001013 <--
     NO 2000005266       A     20001019    NO 2000-5266           20001019 <--
     IN 2000CN00656      A     20050304    IN 2000-CN656          20001113
     HR 2000000776       A1    20010630    HR 2000-776            20001115 <--
     ZA 2000006711       A     20020109    ZA 2000-6711           20001117 <--
PRAI DE 1998-19818614    A     19980420
     WO 1999-EP2618      W     19990419
OS   MARPAT 131:286267
AB   R1XZCONHCHR2COR3 [I; R1 = alkyl, Ph, naphthyl, pyridyl, etc.; R2 = (CH2)mR8;
     R3 = H or CONR6R7; R6,R7 = H or alkyl; R8 = cyclohexyl, Ph, indolyl; X = bond,
     CH2, CH:CH, SO2NH, etc.; Z = carboxyphenylene; m = 1-6] were prepared as
     calpain and cathepsin inhibitors (no data).  Thus, (S)-H2NCH(CH2Ph)CH2OH was
     amidated by monoethyl 5-nitroisophthalate and the reduced product amidated by
     2-naphthalenesulfonyl chloride to give, in 2 addnl. steps, (S)-I (R1 = 2-
     naphthyl, R2 = CH2Ph, R3 = H, X = SO2NH, Z = 1-carboxy-3,5-phenylene).
IT   246856-60-0P 246856-61-1P 246856-64-4P
     246856-65-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of phthalic acid monoamides as calpain and cathepsin
        inhibitors)
RN   246856-60-0  CAPLUS
CN   Benzoic acid, 3-[[[(1S)-1-(hydroxymethyl)-2-phenylethyl]amino]carbonyl]-5-
     [(2-naphthalenylsulfonyl)amino]-, ethyl ester  (CA INDEX NAME)

Absolute stereochemistry.
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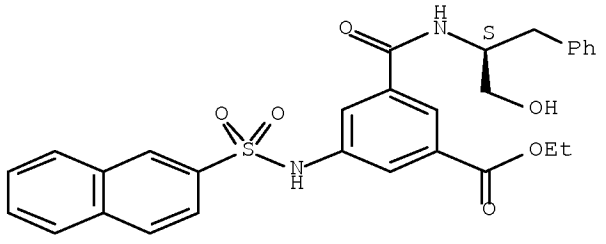


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RN   246856-61-1  CAPLUS
CN   Benzoic acid, 3-[[[(1S)-1-(hydroxymethyl)-2-phenylethyl]amino]carbonyl]-5-
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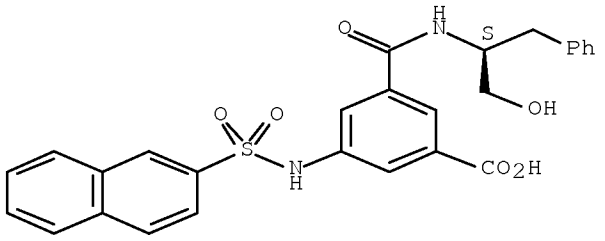
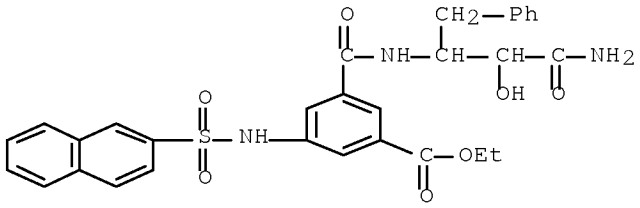
[(2-naphthalenylsulfonyl)amino]- (CA INDEX NAME)

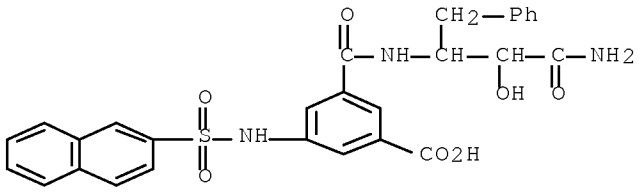
Absolute stereochemistry.



RN 246856-64-4 CAPLUS
CN Benzoic acid, 3-[[[3-amino-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]amino]carbonyl]-5-[(2-naphthalenylsulfonyl)amino]-, ethyl ester (CA INDEX NAME)



RN 246856-65-5 CAPLUS
CN Benzoic acid, 3-[[[3-amino-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]amino]carbonyl]-5-[(2-naphthalenylsulfonyl)amino]- (CA INDEX NAME)

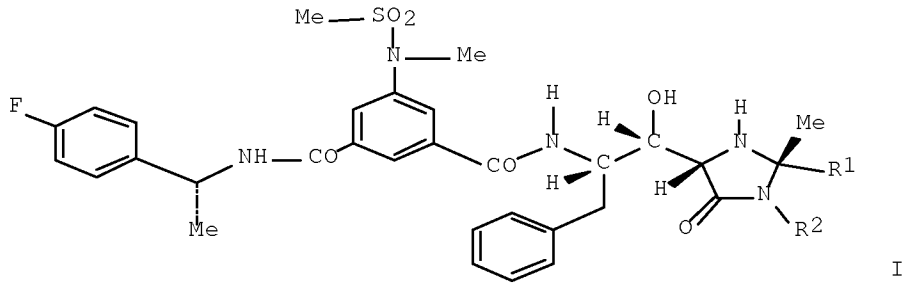


=> s l4 not l5
L6 29 L4 NOT L5

=> dis l6 1-29 bib abs fhitstr

L6 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:808769 CAPLUS Full-text
DN 147:365439
TI Design and synthesis of 2,3,5-substituted imidazolidin-4-one inhibitors of BACE-1
AU Barrow, James C.; Rittle, Kenneth E.; Ngo, Phung L.; Selnick, Harold G.; Graham, Samuel L.; Pitzenberger, Steven M.; McGaughey, Georgia B.;

Colussi, Dennis; Lai, Ming-Tain; Huang, Qian; Tugusheva, Katherine; Espeseth, Amy S.; Simon, Adam J.; Munshi, Sanjeev K.; Vacca, Joseph P.
CS Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA
SO ChemMedChem (2007), 2(7), 995-999
CODEN: CHEMGX; ISSN: 1860-7179
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
GI



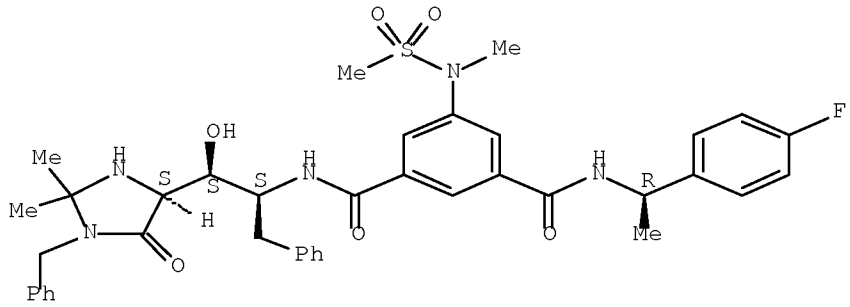
I

AB 2,3,5-Substituted imidazolidin-4-ones (e.g. I (R1 = Me, H; R2 = Bn)) were prepared and tested as BACE-1 inhibitors. The illustrated I are the most potent inhibitors. The crystal and mol. structures of I (R1 = Me; R2 = Me) in the active site of BACE-1 were determined by x-ray crystallog.

IT 949595-63-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(1 of 2 most potent inhibitors; design and synthesis of 2,3,5-substituted imidazolidin-4-one inhibitors of BACE-1 and crystal structure of imidazolidine in active site of β-secretase)

RN 949595-63-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N1-[(1S,2S)-2-[(4S)-2,2-dimethyl-5-oxo-1-(phenylmethyl)-4-imidazolidinyl]-2-hydroxy-1-(phenylmethyl)ethyl]-N3-[(1R)-1-(4-fluorophenyl)ethyl]-5-[methyl(methylsulfonyl)amino]- (CA INDEX NAME)

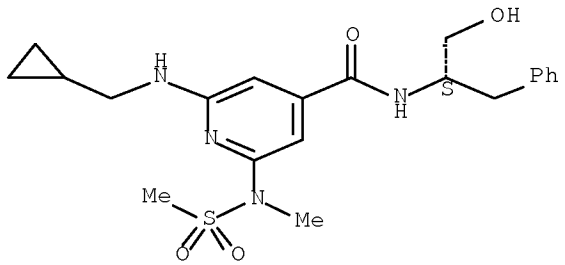
Absolute stereochemistry.



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:664102 CAPLUS Full-text
DN 147:268319
TI Discovery of Isonicotinamide Derived β-Secretase Inhibitors: In Vivo Reduction of β-Amyloid
AU Stanton, Matthew G.; Stauffer, Shaun R.; Gregro, Alison R.; Steinbeiser, Melissa; Nantermet, Philippe; Sankaranarayanan, Sethu; Price, Eric A.; Wu, Guoxin; Crouthamel, Ming-Chih; Ellis, Joan; Lai, Ming-Tain; Espeseth, Amy S.; Shi, Xiao-Ping; Jin, Lixia; Colussi, Dennis; Pietrak, Beth; Huang, Qian; Xu, Min; Simon, Adam J.; Graham, Samuel L.; Vacca, Joseph P.; Selnick, Harold
CS Departments of Medicinal Chemistry, Alzheimer's Research, and Drug Metabolism, Merck Research Laboratories, West Point, PA, 19486, USA
SO Journal of Medicinal Chemistry (2007), 50(15), 3431-3433
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB β-Secretase inhibition offers an exciting opportunity for therapeutic intervention in the progression of Alzheimer's disease. A series of isonicotinamides derived from traditional aspartyl protease transition state isostere inhibitors has been optimized to yield low nanomolar inhibitors with sufficient penetration across the blood-brain barrier to demonstrate β-amyloid lowering in a murine model.
IT 860310-75-4P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(isonicotinamide derivs. as β-secretase inhibitors and in vivo reduction of β-amyloid)
RN 860310-75-4 CAPLUS
CN 4-Pyridinecarboxamide, 2-[(cyclopropylmethyl)amino]-N-[(1S)-1-(hydroxymethyl)-2-phenylethyl]-6-[methyl(methylsulfonyl)amino]- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:585478 CAPLUS Full-text
DN 147:30947
TI Preparation of 2-hydroxy-1,3-diaminoalkanes including spiro substituted chroman derivatives as β-secretase modulators and their use for treatment Alzheimer's disease and related condition

IN Xue, Qiufen; Albrecht, Brian K.; Andersen, Denise Lyn; Bartberger, Michael; Brown, James; Brown, Ryan; Chaffee, Stuart C.; Cheng, Yuan; Croghan, Michael; Graceffa, Russell; Harried, Scott; Hitchcock, Stephen; Hungate, Randall; Judd, Ted; Kaller, Matthew; Kreiman, Charles; La, Daniel; Lopez, Patricia; Masse, Craig E.; Monenschein, Holger; Nguyen, Thomas; Nixey, Thomas; Patel, Vinod F.; Pennington, Lewis; Weiss, Matthew; Yang, Bryant; Zhong, Wenge

PA Amgen Inc., USA

SO PCT Int. Appl., 133pp.
CODEN: PIXXD2

DT Patent

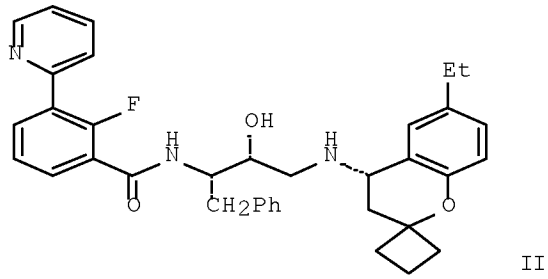
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007061930	A1	20070531	WO 2006-US44833	20061117
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	US 2007173521	A1	20070726	US 2006-599901	20061114
PRAI	US 2005-738766P	P	20051121		
	US 2006-599901	A	20061114		

OS MARPAT 147:30947

GI



II

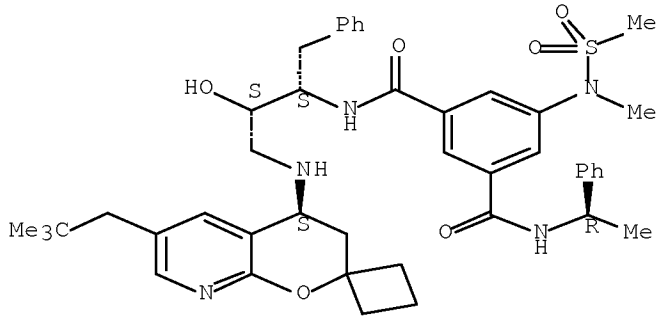
AB The invention is related to a new class of compds R1WNHCH(B)CH(OH)(CR3R3)nNR4(CH2)mR5 [I; R1 = partially or fully saturated (un)substituted 3-8 membered monocyclyl, 6-12 membered bicyclyl, 7-14 membered tricyclyl, optionally containing at least one heteroatom; W = CO, OC(:O), NHCO, SO, SO2, NHSO, NHSO2; B = (CH2)qR2 and derivs., (CH2)qOR2 and derivs., (CH2)qSR2 and derivs., (CH2)qNHR2 and derivs.; R2 = R1, alk(en/yn)yl, haloalkyl; q = 0-3; n = 1-3; m = 0-2; each R3, R4 = independently H, haloalkyl, alkynyl, etc.; R5 = 2,2-spirocycloalkylchroman- 4-yl, 2,2-spirocycloalkylpyrano[2,3-b]pyridin-4-yl, 3,4- dihydrospiro[chromene-2,1'-cycloalkane], etc.; with provisos], their stereoisomers, tautomers, solvates, pharmaceutically acceptable salts, derivs., and prodrugs, and to their

pharmaceutical compns. useful for the modulation of β-secretase enzyme activity and for the treatment of β-secretase mediated diseases, including Alzheimer's disease (AD) and related conditions. Thus, reacting 3-bromo-2-fluorobenzoic acid with iodomethane, followed by coupling of the bromide with 2- (tributylstannyl)pyridine, and amidation of the acid with (2R,3S)-3-amino-1-[((S)-6-ethyl-2,2-spirocyclobutylchroman-4-yl)amino]-4- phenylbutan-2-ol gave the spiro compound II. I displayed an IC50 < 5 μM in both an in vitro enzymic BACE FRET assay and in a BACE cell-based assay.

IT 939022-87-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 2-hydroxy-1,3-diaminoalkanes including spiro substituted chroman derivs. as β-secretase modulators)

RN 939022-87-4 CAPLUS
CN 1,3-Benzenedicarboxamide, N1-[(1S,2S)-3-[[(4'S)-6'-(2,2-dimethylpropyl)-3',4'-dihydrospiro[cyclobutane-1,2'-[2H]pyrano[2,3-b]pyridin]-4'-yl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-5-[methyl(methylsulfonyl)amino]-N3-[(1R)-1-phenylethyl]- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:564970 CAPLUS Full-text
DN 147:9914
TI Preparation of imidazolidinone compounds as β-secretase inhibitors for treatment of Alzheimer's disease
IN Barrow, James C.; Rittle, Kenneth E.; Bondiskey, Phung Le
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 83pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007058862	A2	20070524	WO 2006-US43536	20061110
	WO 2007058862	A3	20071011		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

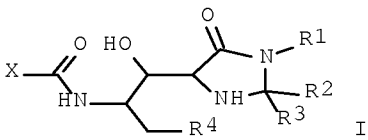
GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

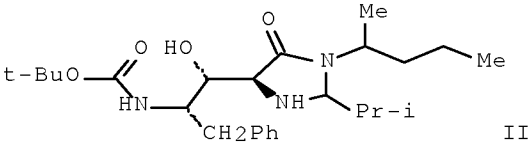
PRAI US 2005-737294P P 20051116

OS MARPAT 147:9914

GI



I



II

AB The title imidazolidinone compds. I [wherein R1-R4 = independently H, (un)substituted alkyl, alkenyl, alkynyl, aryl, or heteroaryl; X = alkyl, alkoxy, etc.] and stereoisomers and pharmaceutically acceptable salts thereof are prepared as inhibitors of β-secretase enzyme for the treatment of diseases in which β-secretase enzyme is involved, such as Alzheimer's disease. For example, the compound II was prepared in a multi-step. I showed inhibitory activities against β-secretase enzyme in an ECL assay with IC50 of 1-100 nM.

IT 937396-14-0P

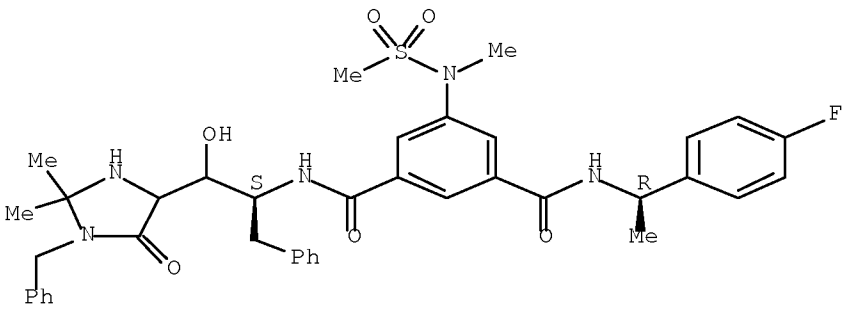
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of imidazolidinone compds. as β-secretase inhibitors for treatment of Alzheimer's disease)

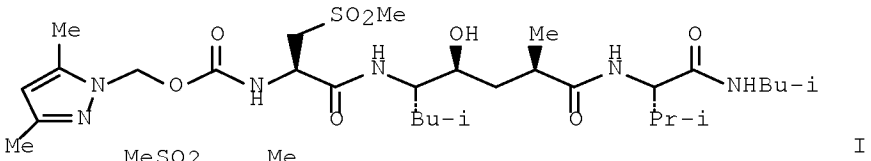
RN 937396-14-0 CAPLUS

CN 1,3-Benzenedicarboxamide, N1-[(1S)-2-[2,2-dimethyl-5-oxo-1-(phenylmethyl)-4-imidazolidinyl]-2-hydroxy-1-(phenylmethyl)ethyl]-N3-[(1R)-1-(4-fluorophenyl)ethyl]-5-[methyl(methylsulfonyl)amino]- (CA INDEX NAME)

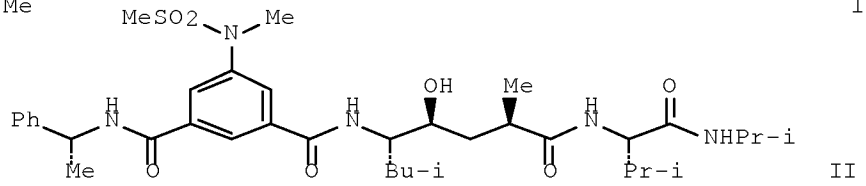
Absolute stereochemistry.



L6 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:414928 CAPLUS Full-text
DN 147:73037
TI Design, Synthesis, and X-ray Structure of Potent Memapsin 2 (β-Secretase) Inhibitors with Isophthalamide Derivatives as the P2-P3-Ligands
AU Ghosh, Arun K.; Kumaragurubaran, Nagaswamy; Hong, Lin; Kulkarni, Sarang S.; Xu, Xiaoming; Chang, Wanpin; Weerasena, Vajira; Turner, Robert; Koelsch, Gerald; Bilcer, Geoffrey; Tang, Jordan
CS Departments of Chemistry and Medicinal Chemistry, Purdue University, West Lafayette, IN, 47907, USA
SO Journal of Medicinal Chemistry (2007), 50(10), 2399-2407
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 147:73037
GI



I



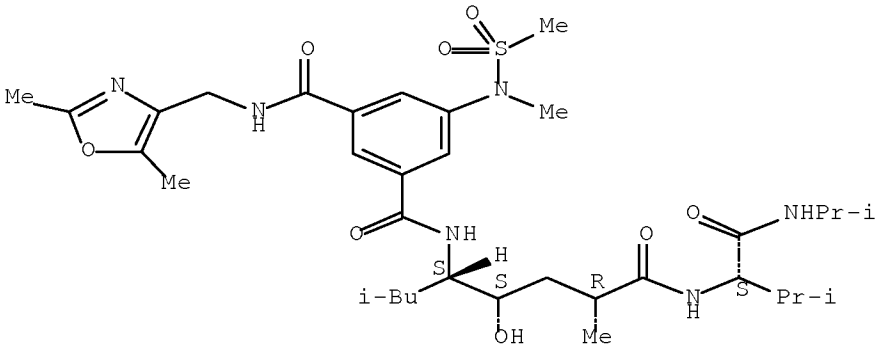
II

AB Structure-based design and synthesis of a number of potent and memapsin 2 (β-secretase)-selective inhibitors are described. These inhibitors were designed based upon the x-ray structure of memapsin 2-bound inhibitor, peptidomimetic I, that incorporates methylsulfonylalanine as the P2-ligand and a substituted pyrazole as the P3-ligand. The authors examined the ability of the substituted isophthalic acid amide derivative to mimic the key interactions in the S2-S3 regions of the enzyme active sites of I-bound memapsin 2. The authors investigated various substituted phenylethyl, α-methylbenzyl, and oxazolylmethyl groups as the P3-ligands. A number of inhibitors exhibited very potent inhibitory activity against memapsin 2 and good selectivity against memapsin 1. For example, isophthalamide-based inhibitor (GRL-7234) II has shown low nanomolar enzyme inhibitory potency (Ki = 1.1 nM) and very good cellular inhibitory activity (IC50 = 39 nM). Furthermore, in a preliminary study, II has shown 30% reduction of Aβ40 production in transgenic mice after a single i.p. administration (8 mg/kg). A protein-ligand x-ray crystal structure of II-bound memapsin 2 provided vital mol. insight that can serve as an important guide to further design of novel inhibitors.

IT 940879-38-9P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(crystal structure of memapsin-2 bound to inhibitor; preparation and memapsin-2-inhibitory activity of isophthalamide derivs. of Leu-Ala

hydroxyethylene dipeptide isosteres)
RN 940879-38-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N1-[(2,5-dimethyl-4-oxazolyl)methyl]-N3-[(1S,2S,4R)-2-hydroxy-4-methyl-5-[[(1S)-2-methyl-1-[[(1-methylethyl)amino]carbonyl]propyl]amino]-1-(2-methylpropyl)-5-oxopentyl]-5-[methyl(methylsulfonyl)amino]- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:283973 CAPLUS Full-text
DN 146:316916
TI Preparation of 3-amino-2-hydroxybutanamide derivatives as β-secretase inhibitors
IN Kiso, Yoshiaki; Mimoto, Tsutomu; Nojima, Satoshi; Kinomura, Naoya
PA Dainippon Sumitomo Pharma Co., Ltd., Japan
SO PCT Int. Appl., 91pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007029587	A1	20070315	WO 2006-JP317178	20060831

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI JP 2005-256427 A 20050905
OS MARPAT 146:316916
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

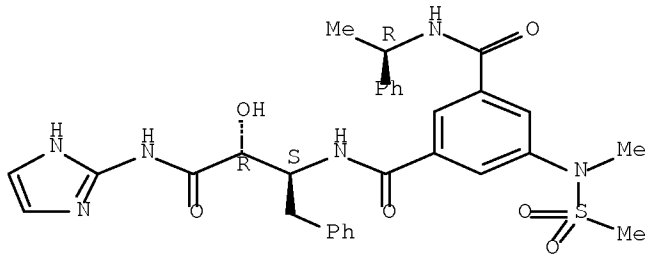
AB Title compds. I [R1 = Q1, etc.; X = N or :C(R5); Y = N or :C(R6); R5, R6 = H, halo, carboxyl, etc.; m = 1-6; L1 = single bond, oxygen or sulfur; R2 = H, optionally substituted alkyl, optionally substituted cycloalkyl, etc.; R3 = H or optionally substituted alkyl; L2 = single bond, -[C(R12)(R13)]q-, -CO-, etc.; R12, R13 = H or optionally substituted alkyl; q = 1-6; R4 = H, optionally substituted (un)saturated aliphatic heterocycle, optionally substituted aryl, optionally substituted aromatic heterocycle] and their pharmaceutically acceptable salts were prepared For example, WSC·HCl mediated acylation of (2R,3S)-3-amino-2-hydroxy-N- (1H-imidazol-2-yl)-4-phenylbutanamide·2HCl, e.g., prepared from (2R,3S)-3-[(tert-butoxycarbonyl)amino]-2-hydroxy-4-phenylbutanoic acid in 3 steps, with 3-[methyl(methylsulfonyl)amino]-5-([[(1R)-1- phenylethyl]amino]carbonyl)benzoic acid afforded compound II. In β-secretase inhibition assays, the invented compds. herein showed the IC50 values of 10 to 10000 nM. Compds. I are claimed useful for the treatment of Alzheimer's disease.

IT 929041-49-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-amino-2-hydroxybutanamide derivs. as β-secretase inhibitors for treatment of Alzheimer's disease)

RN 929041-49-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N1-[(1S,2R)-2-hydroxy-3-(1H-imidazol-2-ylamino)-3-oxo-1-(phenylmethyl)propyl]-5-[methyl(methylsulfonyl)amino]-N3-[(1R)-1-phenylethyl]- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:228885 CAPLUS Full-text

DN 146:462107

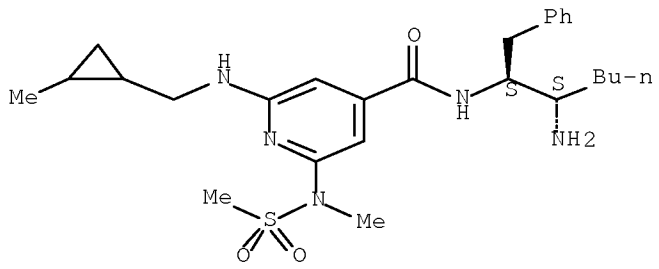
TI Discovery and SAR of isonicotinamide BACE-1 inhibitors that bind β-secretase in a N-terminal 10s-loop down conformation

AU Stauffer, Shaun R.; Stanton, Matthew G.; Gregro, Alison R.; Steinbeiser, Melissa A.; Shaffer, Jennifer R.; Nantermet, Philippe G.; Barrow, James C.; Rittle, Kenneth E.; Collusi, Dennis; Espeseth, Amy S.; Lai, Ming-Tain; Pietrak, Beth L.; Holloway, M. Katharine; McGaughey, Georgia B.; Munshi, Sanjeev K.; Hochman, Jerome H.; Simon, Adam J.; Selnick, Harold G.; Graham, Samuel L.; Vacca, Joseph P.

CS Department of Medicinal Chemistry, Merck Research Laboratories, West

Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (2007), 17(6), 1788-1792
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 146:462107
AB A series of low-mol. weight 2,6-diamino-isonicotinamide BACE-1 inhibitors containing an amine transition-state isostere were synthesized and shown to be highly potent in both enzymic and cell-based assays. These inhibitors contain a trans-S,S-Me cyclopropane P3 which bind BACE-1 in a 10s-loop down conformation giving rise to highly potent compds. with favorable mol. weight and moderate to high susceptibility to P-glycoprotein (P-gp) efflux.
IT 860310-73-2P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, BACE-1 inhibitory and SAR of isonicotinamides using amination of dichloropyridinecarboxylate with sulfonylamides and secondary amines followed by amidation with primary amines as key steps)
RN 860310-73-2 CAPLUS
CN 4-Pyridinecarboxamide, N-[(1S,2S)-2-amino-1-(phenylmethyl)hexyl]-2-[[(2-methylcyclopropyl)methyl]amino]-6-[methyl(methylsulfonyl)amino]- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:175504 CAPLUS Full-text
DN 146:251613
TI Preparation of isophthalamides for the treatment of Alzheimer's disease
IN Fuchs, Klaus; Eickmeier, Christian; Heine, Niklas; Peters, Stefan; Dorner-Ciossek, Cornelia; Handschuh, Sandra; Nar, Herbert; Klinder, Klaus
PA Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma Gmbh & Co. KG
SO PCT Int. Appl., 223pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007017511	A2	20070215	WO 2006-EP65157	20060808
	WO 2007017511	A3	20070426		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

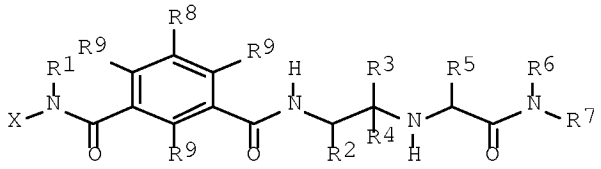
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

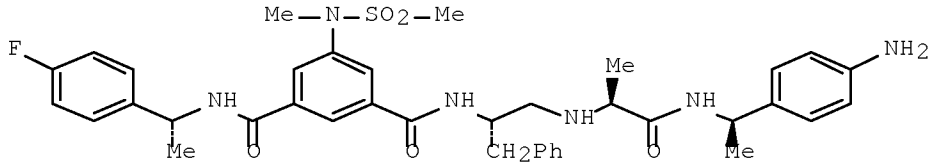
PRAI EP 2005-17475 A 20050811

OS MARPAT 146:251613

GI



I



II

AB Title compds. I [X = B-A-(L)i; B = alkylene with provisos; A = aryl, heteroaryl; L = H, halo, OH, etc.; i = 0-3; R1 = H, alkyl, alkenyl, etc.; R2 = alkyl, alkenyl, alkynyl, etc.; R3, R4 = H, alkyl, F, etc.; R5 = H, alkyl, alkenyl, etc.; R6 = alkenyl, alkynyl, cycloalkyl, etc.; R7 = H, alkyl, alkenyl, etc.] and their pharmaceutically acceptable salts and formulations were prepared For example, isophthalamide II was prepared from Me 2-aminoisophthalate in 9-steps. Compds. I are claimed useful as β-secretase inhibitors.

IT 926018-69-1P

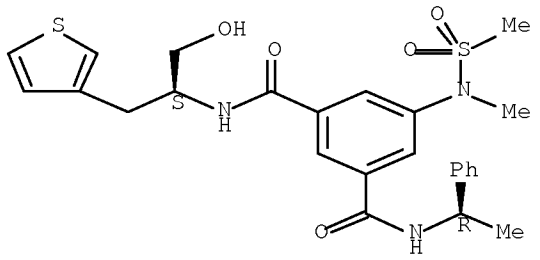
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of isophthalamides for the treatment of Alzheimer's disease)

RN 926018-69-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N1-[(1S)-1-(hydroxymethyl)-2-(3-thienyl)ethyl]-5-[methyl(methylsulfonyl)amino]-N3-[(1R)-1-phenylethyl]- (CA INDEX NAME)

Absolute stereochemistry.

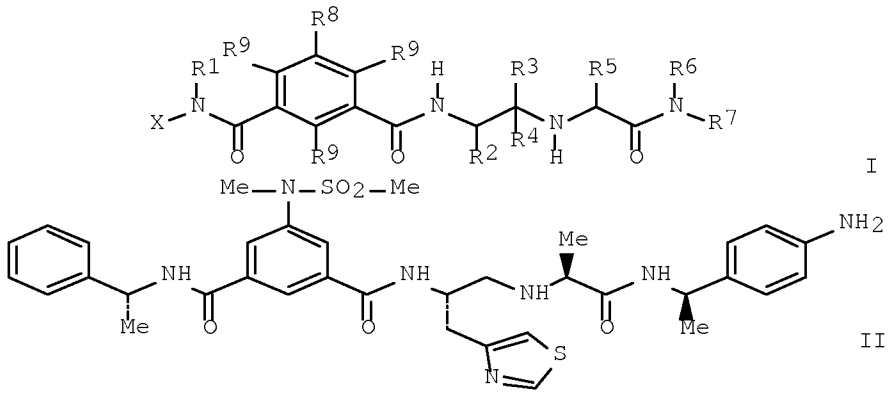


L6 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:175501 CAPLUS Full-text
DN 146:251612
TI Preparation of isophthalamides for the treatment of Alzheimer's disease
IN Heine, Niklas; Fuchs, Klaus; Eickmeier, Christian; Peters, Stefan; Dorner-Ciossek, Cornelia; Handschuh, Sandra; Nar, Herbert; Klinder, Klaus
PA Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma Gmbh & Co. KG
SO PCT Int. Appl., 153pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007017510	A2	20070215	WO 2006-EP65155	20060808

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI EP 2005-17478 A 20050811
OS MARPAT 146:251612
GI



I

II

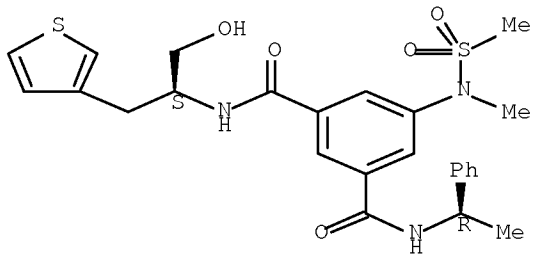
AB Title compds. I [X = B-A-(L)i; B = alkylene with provisos; A = aryl, heteroaryl; L = H, halo, OH, etc.; i = 0-3; R1 = H, alkyl, alkenyl, etc.; R2 = alkyl, alkenyl, alkynyl, etc.; R3, R4 = H, alkyl, F, etc.; R5 = H, alkyl, alkenyl, etc.; R6 = alkenyl, alkynyl, cycloalkyl, etc.; R7 = H, alkyl, alkenyl, etc.] and their pharmaceutically acceptable salts and formulations were prepared For example, the TFA salt of isophthalamide II was prepared from Me 2-aminoisophthalate in 5-steps. Compds. I are claimed useful as β-secretase inhibitors.

IT 926018-69-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isophthalamides for the treatment of Alzheimer's disease)

RN 926018-69-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N1-[(1S)-1-(hydroxymethyl)-2-(3-thienyl)ethyl]-5-[methyl(methylsulfonyl)amino]-N3-[(1R)-1-phenylethyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:146788 CAPLUS Full-text

DN 146:229051

TI Preparation of phenylcarboxamides as β-secretase inhibitors.

IN Wu, Yong-Jin; Zhang, Yunhui

PA USA

SO U.S. Pat. Appl. Publ., 55pp.
CODEN: USXXCO

DT Patent

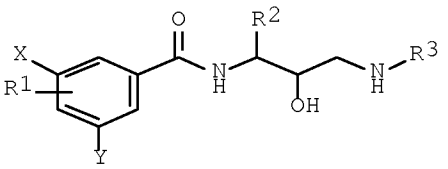
LA English

FAN.CNT 1

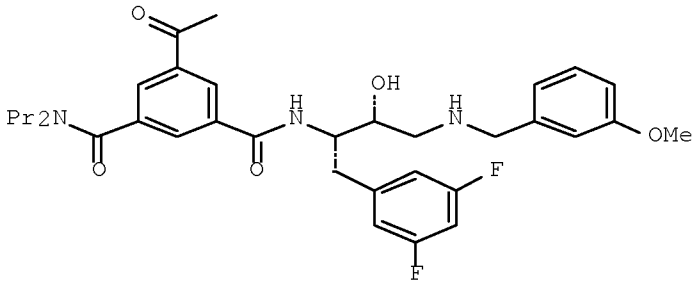
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2007032470	A1	20070208	US 2006-494145	20060727
PRAI	US 2005-705610P	P	20050804		

OS MARPAT 146:229051

GI



I



II

AB Title compds. [I; X = R4CH(OH), R4CO, R4C(:NOR5); Y = CONR6R7, aralkylaminocarbonyl, heteroarylalkylaminocarbonyl, etc.; R1 = H, CF3, alkyl, alkoxy, amino, alkylcarbonylamino, cyano, halo; R2, R3 = aralkyl, heteroarylalkyl; R4, R6, R7 = alkyl; R5 = alkyl, allyl, PhCH2], were prepared Thus, title compound (II) (7-step preparation given) showed activity in a BACE radioligand displacement assay with IC50 <0.1 μM.

IT 924649-27-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of phenylcarboxamides as β-secretase inhibitors)

RN 924649-27-4 CAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]propyl]-3-[methyl(methylsulfonyl)amino]-5-[(1E)-1-[(phenylmethoxy)imino]ethyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

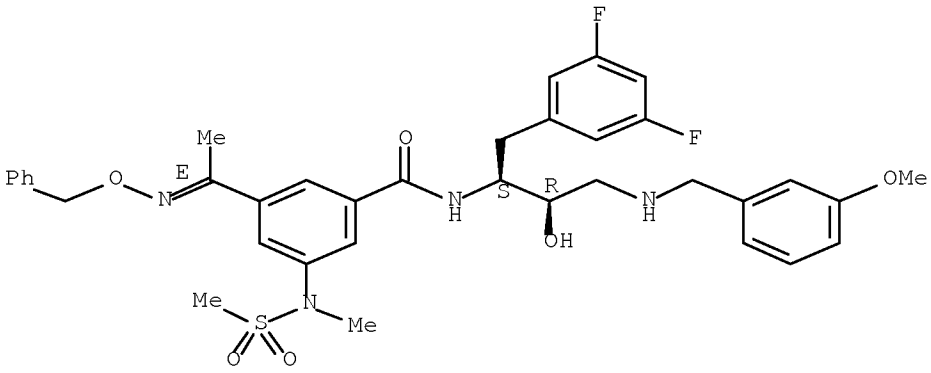
CM 1

CRN 924649-26-3

CMF C36 H40 F2 N4 O6 S

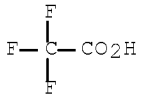
Absolute stereochemistry.

Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



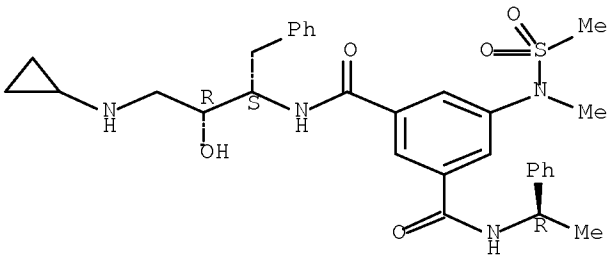
L6 ANSWER 11 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1191598 CAPLUS Full-text
DN 146:116781
TI Discovery of Oxadiazoyl Tertiary Carbinamine Inhibitors of β-Secretase (BACE-1)
AU Rajapakse, Hemaka A.; Nantermet, Philippe G.; Selnick, Harold G.; Munshi, Sanjeev; McGaughey, Georgia B.; Lindsley, Stacey R.; Young, Mary Beth; Lai, Ming-Tain; Espeseth, Amy S.; Shi, Xiao-Ping; Colussi, Dennis; Pietrak, Beth; Crouthamel, Ming-Chih; Tugusheva, Katherine; Huang, Qian; Xu, Min; Simon, Adam J.; Kuo, Lawrence; Hazuda, Daria J.; Graham, Samuel; Vacca, Joseph P.
CS Departments of Medicinal Chemistry, Structural Biology, Molecular Systems and Alzheimer's Research, Merck Research Laboratories, West Point, PA, 19486, USA
SO Journal of Medicinal Chemistry (2006), 49(25), 7270-7273
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 146:116781
AB We describe the discovery and optimization of tertiary carbinamine derived inhibitors of the enzyme β-secretase (BACE-1). These novel non-transition-state-derived ligands incorporate a single primary amine to interact with the catalytic aspartates of the target enzyme. Optimization of this series provided inhibitors with intrinsic and functional potency comparable to evolved transition state isostere derived inhibitors of BACE-1.
IT 797035-11-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(discovery of oxadiazoyl tertiary carbinamine inhibitors of β-secretase)

RN 797035-11-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N1-[(1S,2R)-3-(cyclopropylamino)-2-hydroxy-1-(phenylmethyl)propyl]-5-[methyl(methylsulfonyl)amino]-N3-[(1R)-1-phenylethyl]- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:1149497 CAPLUS Full-text

DN 146:19371

TI Macrocyclic Inhibitors of β-Secretase: Functional Activity in an Animal Model. [Erratum to document cited in CA145:465146]

AU Stachel, Shawn J.; Coburn, Craig A.; Sankaranarayanan, Sethu; Price, Eric A.; Wu, Guoxin; Crouthamel, Michelle; Pietrak, Beth L.; Huang, Qian; Lineberger, Janet; Espeseth, Amy S.; Jin, Lixia; Ellis, Joan; Holloway, M. Katharine; Munshi, Sanjeev; Allison, Timothy; Hazuda, Daria; Simon, Adam J.; Graham, Samuel L.; Vacca, Joseph P.

CS Department of Medicinal Chemistry, Biological Chemistry, Molecular Systems and Structural Biology, Merck Research Laboratories, West Point, PA, 19486, USA

SO Journal of Medicinal Chemistry (2006), 49(24), 7252
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

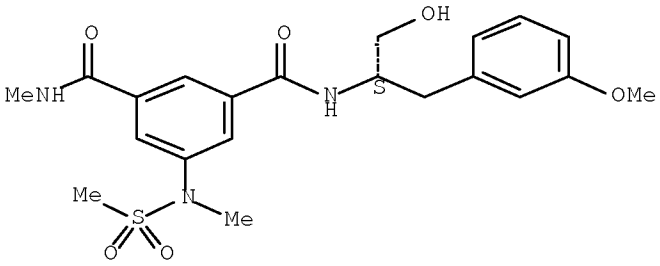
AB Guoxin Wu and Michelle Crouthamel were inadvertently omitted from the author list. Their affiliation is the Department of Biol. Chemical, represented by the double dagger symbol in the paper. The correct author list is given.

IT 913625-93-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model (Erratum))

RN 913625-93-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N1-[(1S)-2-hydroxy-1-[(3-methoxyphenyl)methyl]ethyl]-N3-methyl-5-[methyl(methylsulfonyl)amino]- (CA INDEX NAME)

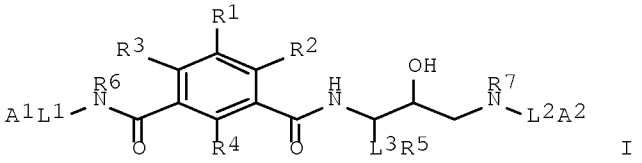
Absolute stereochemistry.



L6 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1094106 CAPLUS Full-text
DN 145:438415
TI Preparation of benzene-1,3-dicarboxamides which inhibit β-secretase activity.
IN Ghosh, Arun K.; Kumaragurubaran, Nagaswamy; Liu, Chunfeng; Devasamudram, Thippeswamy; Lei, Hui; Swanson, Lisa; Ankala, Sudha; Tang, Jordan; Bilcer, Geoffrey
PA Zapaq, Inc., USA; The Board of Trustees of the University of Illinois; Oklahoma Medical Research Foundation
SO PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006110668	A1	20061019	WO 2006-US13342	20060410
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	US 2007117793	A1	20070524	US 2006-463558	20060809
PRAI	US 2005-669541P	P	20050408		
	US 2005-717541P	P	20050914		
	WO 2006-US13342	A1	20060410		

OS MARPAT 145:438415
GI



I

AB Title compds. [I; R1 = H, halo, OH, CF3, NO2, NR8R9, OR10, SOnR11, COR12, (substituted) (hetero)alkyl, cycloalkyl, (hetero)aryl, etc.; R5 = H, halo, OH, CF3, NO2, NR8R9, OR10, SOnR11, COR12, (substituted) (hetero)alkyl, cycloalkyl, (hetero)aryl, etc.; R2, R3 = H, halo, CF3, NO2, NR8R9, OR10, SOnR11, COR12, (substituted) (hetero)alkyl, (hetero)cycloalkyl, (hetero)aryl, etc.; R4 = H, OH, CF3, NO2, NR8R9, OR10, SOnR11, COR12, (substituted) (hetero)alkyl, cycloalkyl, (hetero)aryl, etc.; R6, R7 = H, SO2R11, COR12, NR8R9, (substituted) (hetero)alkyl, cycloalkyl, (hetero)aryl, etc.; n = 0-2; R8 = COR13, SO2R14, H, (substituted) alkyl, etc.; R9 = H, (substituted) heteroalkyl, (hetero)aryl, etc.; R10 = COR13, (substituted) alkyl, (hetero)aryl, etc.; R11 = H, (substituted) (hetero)alkyl, (hetero)aryl, etc.; R12 = H, (substituted) (hetero)alkyl, (hetero)aryl, etc.; R13 = H, (substituted) (hetero)alkyl, (hetero)aryl, etc.; R14 = H, (substituted) (hetero)alkyl, (hetero)aryl, etc.; L1, L3 = bond, S, SO, SO2, (substituted) imino, (hetero)alkylene; L2 = S, SO, SO2, (substituted) (hetero)alkylene, imino; A1, A2 = (substituted) (hetero)cycloalkyl, (hetero)aryl], were prepared Thus, N1-[3-hydroxy-4-(3- methoxybenzylamino)-1-phenylbutan-2-yl]-5-(N-methylmethanesulfonamido)-N3- (1-phenylethyl)isophthalamide (multistep preparation given) inhibited memapsin 2 with Ki <300 nM.

IT 913073-64-0P

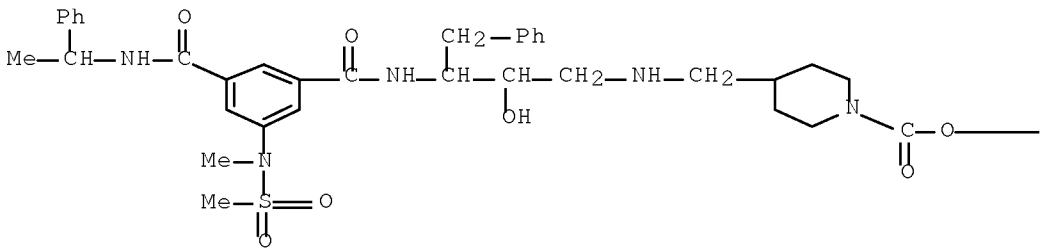
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of benzenedicarboxamides which inhibit β-secretase activity)

RN 913073-64-0 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[[2-hydroxy-3-[[3-[methyl(methylsulfonyl)amino]-5-[[(1-phenylethyl)amino]carbonyl]benzoyl]amino]-4-phenylbutyl]amino]methyl]-, phenylmethyl ester (CA INDEX NAME)

PAGE 1-A



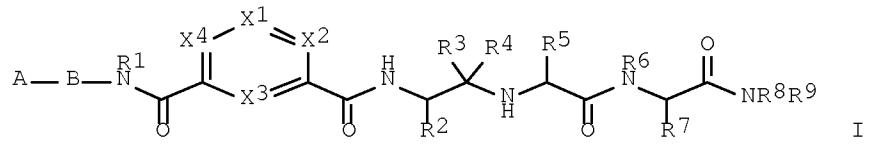
—CH_2—Ph

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

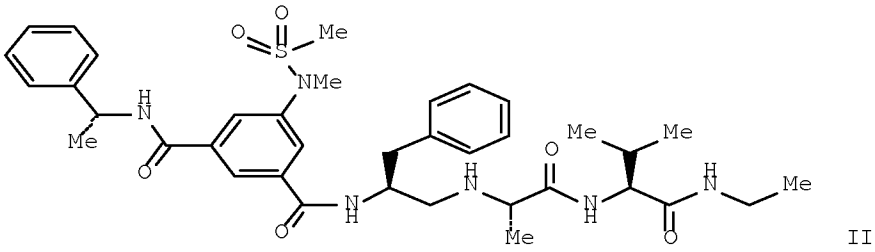
L6 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1041179 CAPLUS Full-text
DN 145:419471
TI Preparation of peptide 1,2-ethylenediamine derivatives for the treatment of Alzheimer's disease
IN Eickmeier, Christian; Fuchs, Klaus; Peters, Stefan; Dorner-Ciossek, Cornelia; Heine, Niklas; Handschuh, Sandra; Klinder, Klaus; Kostka, Marcus
PA Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma Gmbh & Co. KG
SO PCT Int. Appl., 325pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006103038	A1	20061005	WO 2006-EP2769	20060327
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	US 2006223759	A1	20061005	US 2006-278059	20060330
PRAI	EP 2005-6939	A	20050330		

OS MARPAT 145:419471
GI



I



II

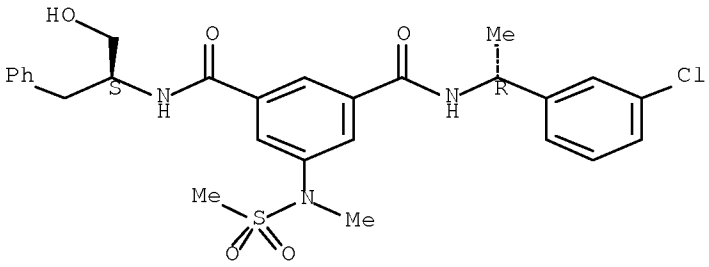
AB The invention relates to substituted 1,2-ethylenediamines I [A is aryl or heteroaryl which may be substituted; B is C1-4-alkylene or oxyalkylene; R1, R2, R5-R9 are H, (un)substituted alkyl, (hetero)aryl, etc. (but R2 is not H); R3, R4 are H, alkyl, F, CF3, CHF2, CH2F; X1-X4 are N, C or substituted carbon (0-3 of these groups are N)], including tautomers, diastereomers, enantiomers, and salts, and their use in the treatment of Alzheimer's disease (AD) and similar diseases. Thus, peptide II was prepared by a multistep sequence using reactants which include di-Me 5-aminoisophthalate, (R)-1-phenylethylamine, and protected amino acids. Compds. of the invention listed in a table have IC50 values < 30 μM in the β-secretase inhibition assay.

IT 911791-05-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide ethylenediamine derivs. for treatment of Alzheimer's disease)

RN 911791-05-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N-[(1R)-1-(3-chlorophenyl)ethyl]-N'-[(1S)-1-(hydroxymethyl)-2-phenylethyl]-5-[methyl(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



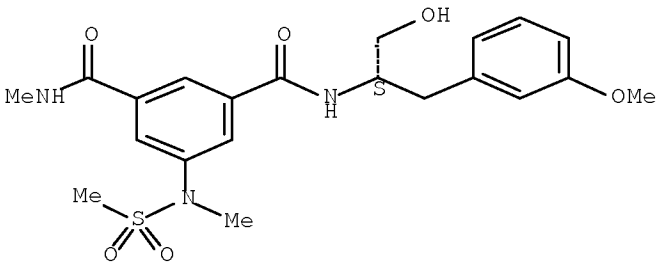
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:908572 CAPLUS Full-text

DN 145:465146
TI Macrocyclic Inhibitors of β-Secretase: Functional Activity in an Animal Model
AU Stachel, Shawn J.; Coburn, Craig A.; Sankaranarayanan, Sethu; Price, Eric A.; Pietrak, Beth L.; Huang, Qian; Lineberger, Janet; Espeseth, Amy S.; Jin, Lixia; Ellis, Joan; Holloway, M. Katharine; Munshi, Sanjeev; Allison, Timothy; Hazuda, Daria; Simon, Adam J.; Graham, Samuel L.; Vacca, Joseph P.
CS Department of Medicinal Chemistry, Biological Chemistry, Molecular Systems and Structural Biology, Merck Research Laboratories, West Point, PA, 19486, USA
SO Journal of Medicinal Chemistry (2006), 49(21), 6147-6150
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 145:465146
AB A macrocyclic inhibitor of β-secretase was designed by covalently crosslinking the P1 and P3 side chains of an isophthalamide-based inhibitor. Macrocyclization resulted in significantly improved potency and phys. properties when compared to the initial lead structures. More importantly, these macrocyclic inhibitors also displayed in vivo amyloid lowering when dosed in a murine model.
IT 913625-93-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model)
RN 913625-93-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N1-[(1S)-2-hydroxy-1-[(3-methoxyphenyl)methyl]ethyl]-N3-methyl-5-[methyl(methylsulfonyl)amino]- (CA INDEX NAME)

Absolute stereochemistry.



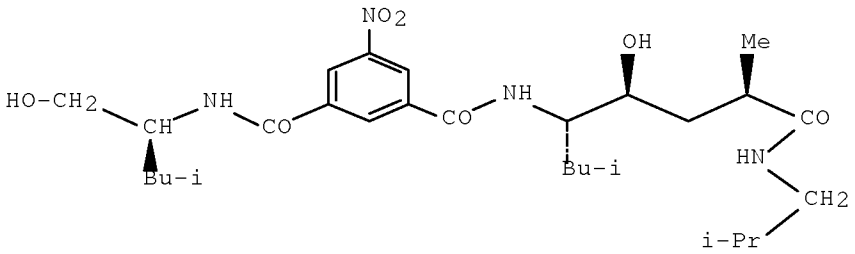
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:505949 CAPLUS Full-text
DN 145:116717
TI Design, synthesis, and evaluation of Leu*Ala hydroxyethylene-based non-peptide β-secretase (BACE) inhibitors
AU Xiao, Kun; Li, Xin; Li, Jingya; Ma, Lanping; Hu, Bin; Yu, Haiping; Fu, Yan; Wang, Rui; Ma, Zeqiang; Qiu, Beiying; Li, Jia; Hu, Dingyu; Wang, Xin; Shen, Jingkang

CS State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Shanghai Institute for Biological Sciences, Graduate School of the Chinese Academy of Sciences, Chinese Academy of Sciences, Shanghai, 201203, Peop. Rep. China

SO Bioorganic & Medicinal Chemistry (2006), 14(13), 4535-4551
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 145:116717

GI



I

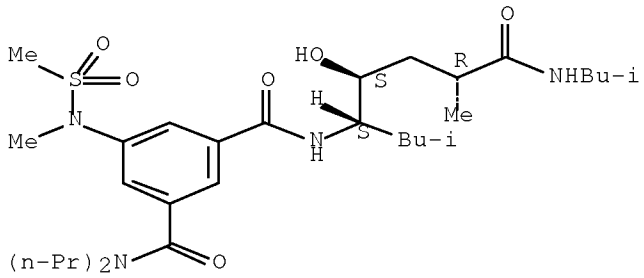
AB With the aim of developing small mol. non-peptide β-secretase (BACE) inhibitors, Leu*Ala hydroxyethylene (HE) was investigated as a scaffold to design and synthesize a series of compds. Taking advantage of efficient combinatorial synthesis approaches and mol. modeling, extensive structure-activity relationship (SAR) studies were carried out on the N- and C-terminal residues of the Leu*Ala HE scaffold. Iso-Bu amine was found to be an optimal C-cap, and suitable hydroxylalkylamines at the 3-position and nitro or methyl(methylsulfonyl)amine at the 5-position of isophthalamide as the N-terminus could form addnl. hydrogen bonds with BACE active sites and help improve potency. Many new potent non-peptide BACE inhibitors were identified in this study. Among them, a couple of compds., including I, exhibited excellent enzyme-inhibiting potency, comparable to that of OM99-2, and obvious inhibitory effects in cell-based assay with low mol. wts. (<600).

IT 897664-09-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Leu/Ala hydroxyethylene-based non-peptide β-secretase inhibitors)

RN 897664-09-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2S,4R)-2-hydroxy-4-methyl-1-(2-methylpropyl)-5-[(2-methylpropyl)amino]-5-oxopentyl]-5-[methyl(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

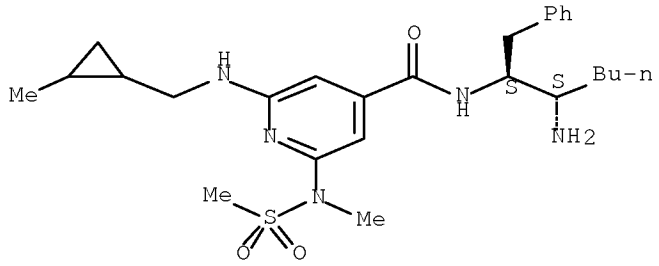
Absolute stereochemistry. Rotation (-).



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:502466 CAPLUS Full-text
DN 145:224304
TI Computational approaches to the prediction of blood-brain barrier permeability: a comparative analysis of central nervous system drugs versus secretase inhibitors for Alzheimer's disease
AU Rishton, Gilbert M.; LaBonte, Kristen; Williams, Antony J.; Kassam, Karim; Kolovanov, Eduard
CS Channel Islands Alzheimer's Institute, California State University Channel Islands, Camarillo, CA, 93012, USA
SO Current Opinion in Drug Discovery & Development (2006), 9(3), 303-313
CODEN: CODDFF; ISSN: 1367-6733
PB Thomson Scientific
DT Journal
LA English
AB This review summarizes progress made in the development of fully computational approaches to the prediction of blood-brain barrier (BBB) permeability of small mols., with a focus on rapid computational methods suitable for the anal. of large compound sets and virtual screening. A comparative anal. using the recently developed Advanced Chemical Development (ACD/Labs) Inc BBB permeability algorithm for the calcn. of logBB values for known Alzheimer's disease medicines, selected central nervous system drugs and new secretase inhibitors for Alzheimer's disease, is presented. The trends in logBB values and the associated physiochem. properties of these agents as they relate to the potential for BBB permeability are also discussed.
IT 860310-73-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(computational approaches to prediction of blood-brain barrier permeability and comparative anal. of central nervous system drugs vs. secretase inhibitors for Alzheimer's disease)
RN 860310-73-2 CAPLUS
CN 4-Pyridinecarboxamide, N-[(1S,2S)-2-amino-1-(phenylmethyl)hexyl]-2-[[(2-methylcyclopropyl)methyl]amino]-6-[methyl(methylsulfonyl)amino]- (CA INDEX NAME)

Absolute stereochemistry.



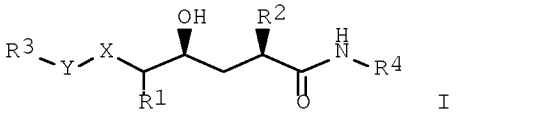
RE.CNT 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:361381 CAPLUS Full-text
DN 145:124332
TI Preparation of 4-hydroxypentanamide derivatives for treatment of senile dementia
IN Shen, Jingkang; Li, Jia; Xiao, Kun; Li, Jingya; Li, Xin; Ma, Zeqiang; Hu, Bin; Yu, Haiping; Wang, Xin; Qiu, Beiying; Hu, Dingyu
PA Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 21 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

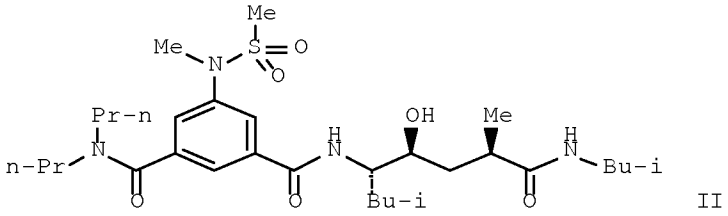
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1757635	A	20060412	CN 2005-10023951	20050218
WO 2006086923	A1	20060824	WO 2006-CN35	20060111

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI CN 2005-10023951 A 20050218
OS CASREACT 145:124332; MARPAT 145:124332
GI



I



II

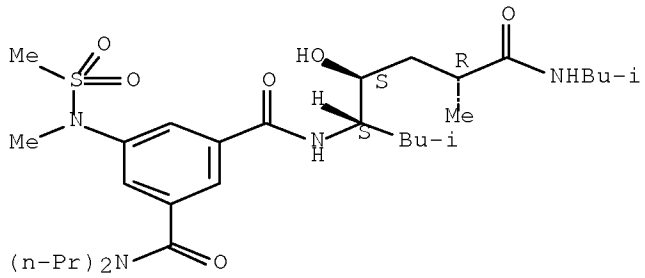
AB The title compds. I [wherein R1 = H, alkyl, benzyl, etc.; R2 = H or alkyl; R4 = alkyl, cycloalkyl, etc.; R3 = (un)substituted Ph or pyridinyl; X = NH, O, or CH2; Y = CO, SO, or CH2] are prepared as protease inhibitors for the treatment of senile dementia. For example, the compound II was prepared in a multi-step synthesis. I showed good inhibitory activity against proteinase.

IT 897664-09-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-hydroxypentanamide derivs. for treatment of senile dementia)

RN 897664-09-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2S,4R)-2-hydroxy-4-methyl-1-(2-methylpropyl)-5-[(2-methylpropyl)amino]-5-oxopentyl]-5-[methyl(methylsulfonyl)amino]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L6 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:298659 CAPLUS Full-text

DN 144:350978

TI Preparation of pseudopeptides which inhibit β-secretase activity

IN Ghosh, Arun; Lei, Hui; Devasamudram, Thippeswamy; Liu, Chunfeng; Tang, Jordan; Bilcer, Geoffrey

PA Zapaq, Inc., USA; The Board of Trustees of the University of Illinois; Oklahoma Medical Research Foundation

SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2

DT Patent

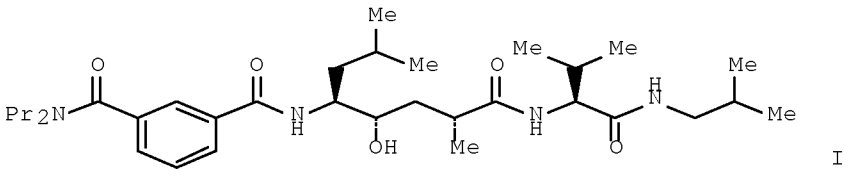
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006034277	A1	20060330	WO 2005-US33678	20050919
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	AU 2005286844	A1	20060330	AU 2005-286844	20050919
	CA 2580238	A1	20060330	CA 2005-2580238	20050919
	EP 1797052	A1	20070620	EP 2005-812011	20050919
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI	US 2004-610874P	P	20040917		
	WO 2005-US33678	W	20050919		

OS MARPAT 144:350978

GI



I

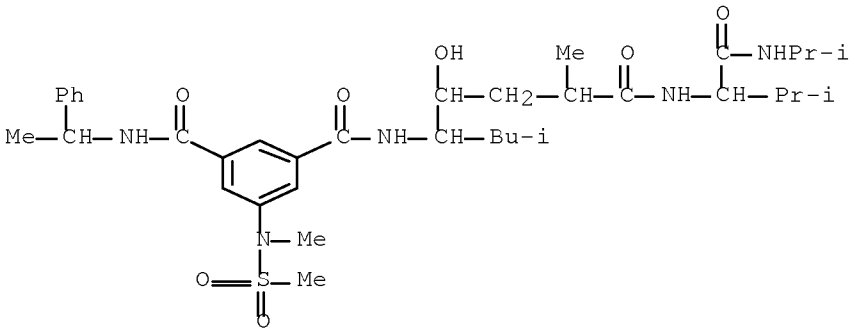
AB The invention provides compds. A6-L6-A5-L5-(CHR2)nCONHCH(L1-R1)CH(OH)CH2CH(L3-R3)CONR5-L4-R4 [n is 0 or 1; A5 is (un)substituted cycloalkylene, heterocycloalkylene, arylene or heteroarylene; A6 is (un)substituted cycloalkyl, heterocycloalkyl, aryl or heteroaryl; R1, R3 are independently amino groups, OH, alkoxy, acyl, N3, H, alkyl, aryl, amino acid side chain, etc.; R2, R4, R5 are independently H, (un)substituted alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl or -L7-Y, where L7 is a bond, OP(OH)2O, carboxylic ester, etc. and Y is a carrier moiety; L1, L3 are independently (un)substituted alkylene or heteroalkylene; L4 is a bond, CO, (un)substituted alkylene or heteroalkylene; L5, L6 are independently a bond, CO, O, imino, S, (un)substituted alkylene or heteroalkylene, etc.] which are β-secretase inhibitors for use in treating Alzheimer's disease. The synthesis of exemplary isostere inhibitor I is described. A table shows Ki values for inhibition of memapsin 2 β-secretase and cathepsin D activities by compds. of the invention.

IT 881477-57-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

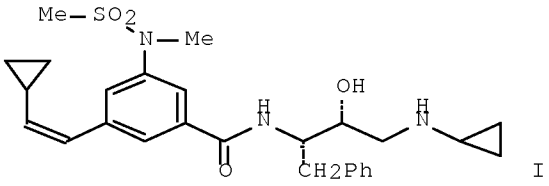
(preparation of pseudopeptides which inhibit β-secretase activity)

RN 881477-57-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[2-hydroxy-4-methyl-5-[[2-methyl-1-[[(1-methylethyl)amino]carbonyl]propyl]amino]-1-(2-methylpropyl)-5-oxopentyl]-5-[methyl(methylsulfonyl)amino]-N'-(1-phenylethyl)- (9CI) (CA INDEX NAME)



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1341977 CAPLUS Full-text
DN 144:232776
TI Conformationally biased P3 amide replacements of β-secretase inhibitors
AU Stachel, Shawn J.; Coburn, Craig A.; Steele, Thomas G.; Crouthamel, Min-Chi; Pietrak, Beth L.; Lai, Ming-Tain; Holloway, M. Katharine; Munshi, Sanjeev K.; Graham, Samuel L.; Vacca, Joseph P.
CS Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(3), 641-644
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 144:232776
GI



I

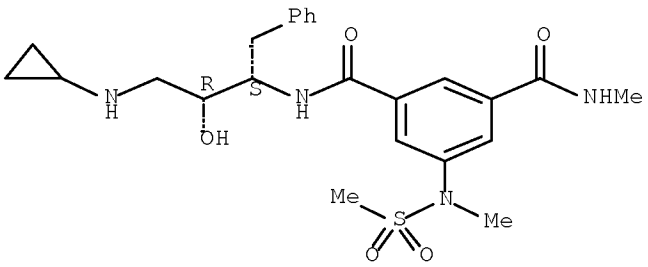
AB A series of conformationally biased P3 amide replacements based on an isophthalamide lead structure were synthesized and evaluated. The studies resulted in the identification of the β-secretase inhibitor I which has an in vitro IC50 = 35 nM. The synthesis and biol. activities of these compds. are described.
IT 876593-29-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of conformationally biased P3 amide replacements of β-secretase inhibitors)

RN 876593-29-2 CAPLUS

CN 1,3-Benzenedicarboxamide, N-[(1S,2R)-3-(cyclopropylamino)-2-hydroxy-1-(phenylmethyl)propyl]-N'-methyl-5-[methyl(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:1220126 CAPLUS Full-text

DN 143:477844

TI Preparation of acylated 2-amino-1-(pyrrolidin-2-yl)ethanols and derivatives as BACE inhibitors for treating Alzheimer's

IN Dally, Robert Dean; Shepherd, Timothy Alan; Bender, David Michael; Rojo Garcia, Maria Isabel

PA Eli Lilly and Company, USA

SO PCT Int. Appl., 193 pp.
CODEN: PIXXD2

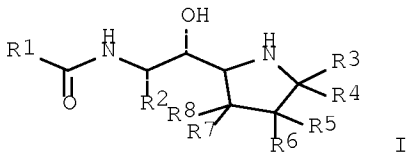
DT Patent

LA English

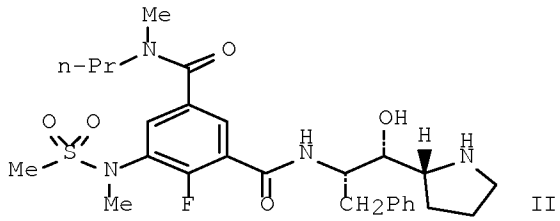
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005108358	A2	20051117	WO 2005-US12191	20050408
	WO 2005108358	A3	20060526		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1740575	A2	20070110	EP 2005-778064	20050408
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	US 2007213331	A1	20070913	US 2006-599129	20060920

PRAI US 2004-564538P P 20040422
WO 2005-US12191 W 20050408
OS MARPAT 143:477844
GI



I



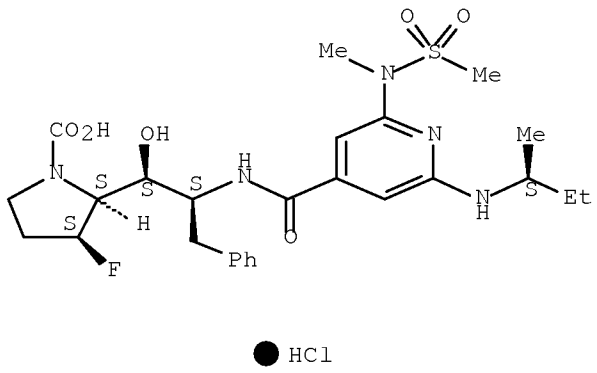
II

AB Title compds. I [R1 = biphenyl substituted with halo, (un)substituted cycloalkyl/alk(en/yn)yl, cycloalkyl; R2 = alkyl, (un)substituted benzyl; R3 = H, alkyl; R4 = H, alkyl, Ph; R3CR4 = cycloalkyl ring; R5 = H, F, CF3, (un)substituted Ph; R6 = F, OH, OTs, , etc.; R5R6 = :CHC(:O)-alkoxy; R7 = H, F; R6 and R7 taken together for a bond; R8 = H, F; and their pharmaceutically acceptable salts; with provisos] were prepared as β-site APP-cleaving enzyme (BACE) inhibitors. Thus, amidation of 6-Fluoro-5-[(methylsulfonyl)(methyl)amino]-N-methyl-N-propylisophthalamic acid (preparation given) with (R)-2-((1S,2S)-2-Amino-1-hydroxy-3-phenylpropyl)pyrrolidine-1-carboxylic acid tert-Bu ester and Boc-deprotection gave II•HCl. I exhibited an IC50 for BACE1 and BACE2 of at least 15 μM in a BACE1 and BACE2 mcaFRET assay. Thus, I are useful for treating Alzheimer's disease and preventing progressive of mild cognitive impairment to Alzheimer's disease.

IT 869530-30-3P, 2-(S)-[2-[[[2-[((1S)-1-Methylpropyl)amino]-6-[(methylsulfonyl)(methyl)amino]pyridin-4-yl]carbonyl]amino]-1-(S)-hydroxy-3-phenylpropyl]-3-(S)-fluoropyrrolidine-1-carboxylic acid hydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of amides as BACE inhibitors for treating Alzheimer's)

RN 869530-30-3 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-fluoro-2-[(1S,2S)-1-hydroxy-2-[[[2-[methyl(methylsulfonyl)amino]-6-[[(1S)-1-methylpropyl]amino]-4-pyridinyl]carbonyl]amino]-3-phenylpropyl]-, monohydrochloride, (2S,3S)-(9CI) (CA INDEX NAME)

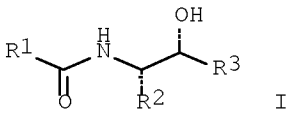
Absolute stereochemistry.



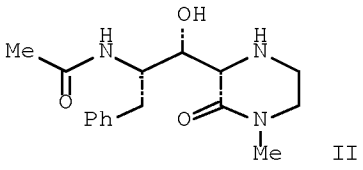
L6 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1220116 CAPLUS Full-text
DN 143:477983
TI Preparation of amides as BACE inhibitors for treating Alzheimer's
IN Bueno Melendo, Ana Belen; Chen, Shu-Hui; Erickson, Jon Andre; Gonzalez-Garcia, Maria Rosario; Guo, Deqi; Marcos Llorente, Alicia; McCarthy, James Ray; Shepherd, Timothy Alan; Sheehan, Scott Martin; Yip, Yvonne Yee Mai
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 212 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005108391	A1	20051117	WO 2005-US12189	20050408
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1740573	A1	20070110	EP 2005-736358	20050408
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	US 2007225372	A1	20070927	US 2006-599125	20060920
PRAI	US 2004-564538P	P	20040422		
	WO 2005-US12189	W	20050408		

OS MARPAT 143:477983
GI



I



II

AB Title compds. I [R1 = (un)substituted cycloalkyl/alkyl, biphenyl, cycloalkyl, etc.; R2 = alkyl, (un)substituted benzyl; R3 = (un)substituted piperidin-2-yl, tetrahydropyridin-2-yl, piperazin-2-yl, homopiperidin-2-yl, etc.] were prepared as β-site APP-cleaving enzyme (BACE) inhibitors. Thus, acetylation of 3-(S)-(2-(S)-amino-1-(S)-hydroxy- 3-phenylpropyl)-1-methylpiperazin-2-one (preparation given) with AcOH gave amide II•HCl. I exhibited an IC50 for BACE1 and BACE2 of at least 15 μM in a BACE1 and BACE2 mcaFRET assay. Thus, I are useful for treating Alzheimer's disease and preventing progressive of mild cognitive impairment to Alzheimer's disease.

IT 869658-88-8P

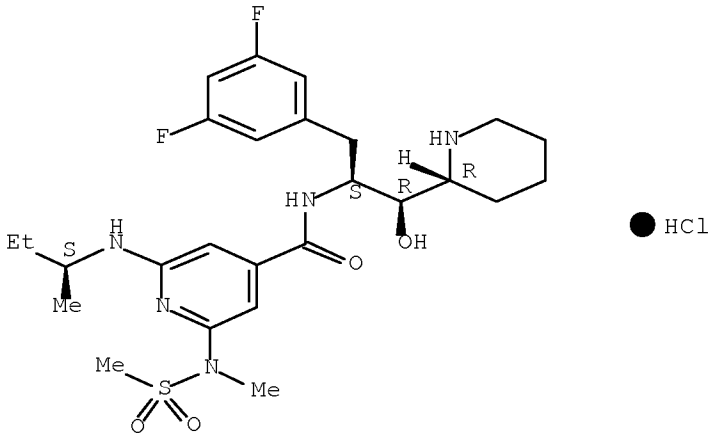
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of amides as BACE inhibitors for treating Alzheimer's)

RN 869658-88-8 CAPLUS

CN 4-Pyridinecarboxamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-2-(2R)-2-piperidinylethyl]-2-[methyl(methylsulfonyl)amino]-6-[[(1S)-1-methylpropyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:638626 CAPLUS Full-text
DN 143:153293
TI Preparation of phenylamides and pyridylamides as β-secretase inhibitors
IN Barrow, James C.; Coburn, Craig A.; Nantermet, Philippe G.; Selnick, Harold G.; Stachel, Shawn J.; Stanton, Matthew G.; Stauffer, Shaun R.; Zhuang, Linghang; Davis, Jennifer R.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005065195	A2	20050721	WO 2004-US42173	20041215
	WO 2005065195	A3	20060406		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004311749	A1	20050721	AU 2004-311749	20041215
	CA 2548849	A1	20050721	CA 2004-2548849	20041215
	EP 1697308	A2	20060906	EP 2004-814367	20041215
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
	CN 1898199	A	20070117	CN 2004-80038063	20041215
	JP 2007517781	T	20070705	JP 2006-545405	20041215
	IN 2006DN02139	A	20070629	IN 2006-DN2139	20060419
	US 2007142634	A1	20070621	US 2006-582856	20060614
PRAI	US 2003-531423P	P	20031219		
	WO 2004-US42173	W	20041215		

OS MARPAT 143:153293
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

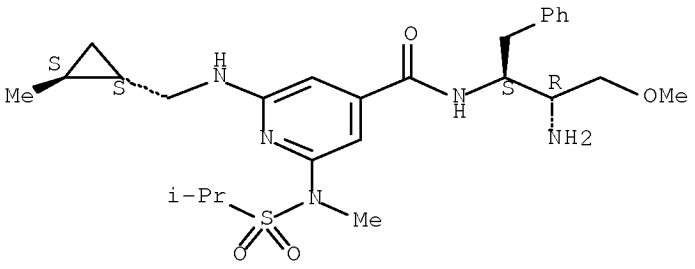
AB Title compds. I [Y = CH or N; Q1 = OH or NH2; Q2 and Q3 independently = H or halo; Ra = H, cycloalkyl, (un)substituted alkyl; Rb = H, (un)substituted alkyl, cycloalkyl, etc.; m = 1-2; R1 = (un)substituted aryl, heteroaryl, alkyl, etc.; R2 = (R4-SO2)N(R5); R3 = R6R7CHNHCO; R8R9NCO; R10R11N, etc.; R4 = (un)substituted alkyl, cycloalkyl, heteroaryl, etc.; R5 = H, (un)substituted alkyl, aryl, etc., or R4 and R5 together form sulfurheterocycle containing optionally one more nitrogen atom; R6 = alkyl or perfluoroalkyl; R7 = (un)substituted aryl or pyridyl; R8 and R9 independently = H, (un)substituted alkyl, cycloalkyl, or R8 and R9 together with the nitrogen atom to which they are attached form (un)substituted heterocycle; R10 = (un)substituted alkyl, cycloalkyl, -(CH2)x-Ph, etc.; x = 1-4; R11 = H, (un)substituted alkyl, cycloalkyl] and their pharmaceutically acceptable salts, are prepared and

disclosed as β-secretase inhibitors. Thus, e.g., II was prepared by amidation of 2-{[(2-methylcyclopropyl)methyl]amino}-6-[methyl(methylsulfonyl)amino]isonicotinic acid (preparation given) with (2S,3S)-3-azido-1-phenylheptan-2-amine (preparation given) and subsequent reduction The activity of I was evaluated in a homogeneous end point fluorescence resonance energy transfer (FRET) assay and it was revealed that compds. of the invention generally had an inhibitory capability towards β-secretase enzyme with an IC50 value from about 1 nM to 100 μM. I as β-secretase inhibitors should prove useful in the treatment of Alzheimer's disease. Pharmaceutical compns. comprising I are disclosed.

IT 860312-31-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of phenylamides and pyridylamides as β-secretase inhibitors)

RN 860312-31-8 CAPLUS
CN 4-Pyridinecarboxamide, N-[(1S,2R)-2-amino-3-methoxy-1-(phenylmethyl)propyl]-2-[[[(1S,2S)-2-methylcyclopropyl]methyl]amino]-6-[methyl[(1-methylethyl)sulfonyl]amino]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:525744 CAPLUS Full-text
DN 143:207999
TI Biochemical and cell-based assays for characterization of BACE-1 inhibitors
AU Pietrak, Beth L.; Crouthamel, Ming-Chih; Tugusheva, Katherine; Lineberger, Janet E.; Xu, Min; DiMuzio, Jillian M.; Steele, Thomas; Espeseth, Amy S.; Stachel, Shawn J.; Coburn, Craig A.; Graham, Samuel L.; Vacca, Joseph P.; Shi, Xiao-Ping; Simon, Adam J.; Hazuda, Daria J.; Lai, Ming-Tain
CS Department of Biological Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA
SO Analytical Biochemistry (2005), 342(1), 144-151
CODEN: ANBCA2; ISSN: 0003-2697
PB Elsevier
DT Journal
LA English
AB The deposition of β-amyloid peptides (Aβ42 and Aβ40) in neuritic plaques is one of the hallmarks of Alzheimer's disease (AD). Aβ peptides are derived from sequential cleavage of amyloid precursor protein (APP) by β- and γ-secretases. BACE-1 has been shown to be the major β-secretase and is a primary therapeutic target for AD. In this article, two novel assays for the characterization of BACE-1 inhibitors are reported. The first is a sensitive 96-well HPLC biochem. assay that uses a unique substrate containing an optimized peptide

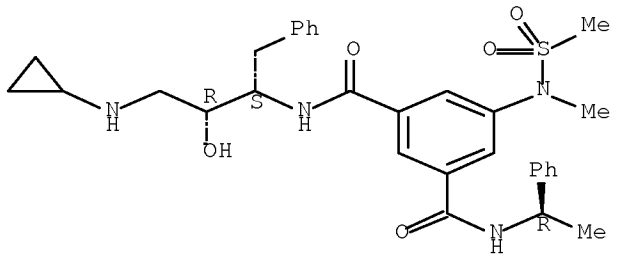
cleavage sequence, NFEV, spanning from the P2-P2' positions. This substrate was processed by BACE-1 approx. 10 times more efficiently than was the widely used substrate containing the Swedish (NLDA) sequence. As a result, the concentration of the enzyme required for the assay can be as low as 100 pM, permitting the evaluation of inhibitors with subnanomolar potency. The assay has also been applied to related aspartyl proteases such as cathepsin D (Cat D) and BACE-2. The second assay is a homogeneous electrochemiluminescence assay for the evaluation of BACE-1 inhibition in cultured cells that assesses the level of secreted amyloid EV40_NF from HEK293T cells stably transfected with APP containing the novel NFEV sequence. To illustrate the use of these assays, the properties of a potent, cell-active BACE-1 inhibitor are described.

IT 797035-11-1
RL: BSU (Biological study, unclassified); BIOL (Biological study) (biochem. and cell-based assays for characterization of BACE-1 inhibitors)

RN 797035-11-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N1-[(1S,2R)-3-(cyclopropylamino)-2-hydroxy-1-(phenylmethyl)propyl]-5-[methyl(methylsulfonyl)amino]-N3-[(1R)-1-phenylethyl]- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:300397 CAPLUS Full-text
DN 142:373564
TI Preparation of sulfone amide derivatives as inhibitors of β-secretase
IN Oh, Yeong Soo; Choi, Deog-young; Cho, Young Lag; Yoon, Sook Kyung; Seo, Sang Won; Lim, Dongchul; Min, Kyeongsik; Lee, Tae-soo; Lee, Sun Hwa; Chung, Kyung Ha; Kim, Byeong Moon; Bae, Sung Jin; Lee, Jong Sun; Lee, Dae-won; Jeong, Moses
PA Lg Life Sciences Ltd., S. Korea; Promeditech, Inc.
SO PCT Int. Appl., 251 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005030709	A1	20050407	WO 2004-KR2523	20041001

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO,

NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

KR 2005032177 A 20050407 KR 2003-68187 20031001
PRAI KR 2003-68187 A 20031001
OS MARPAT 142:373564
GI

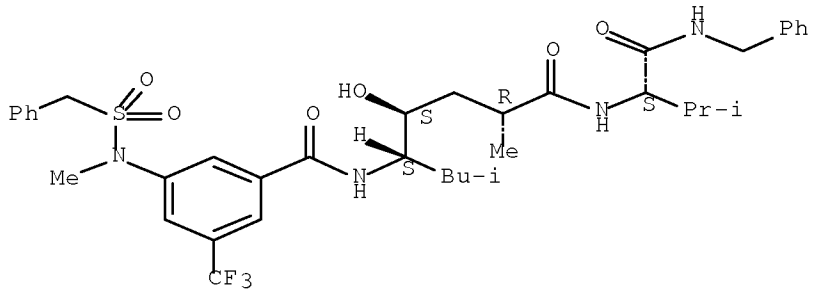
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [A = H, halo, CN, etc.; R1-3 = alkyl, etc.; X = substituted alkyl, oxazolyl, etc.] are prepared For instance, II is prepared in 5 steps from (2R,4S,5S)-4-((tert-butyldimethylsilyl)oxy)-5-[(3-(1,1-dioxoisothiazolidin-2-yl)benzoyl)amino]-2,7-dimethyloctanoic acid (preparation given), 4-(((tert-butoxycarbonyl)amino)methyl)benzoic acid, benzyl bromide, N-BocAlanine. IC50 against β-secretase for compds. of the invention is in the range of 0.5 - 50 μM. I are useful for the treatment of Alzheimer's disease and related diseases caused by production of beta-amyloid.

IT 849408-45-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfone amide derivs. as inhibitors of β-secretase)

RN 849408-45-3 CAPLUS
CN Benzamide, N-[(1S,2S,4R)-2-hydroxy-4-methyl-5-[[(1S)-2-methyl-1-[[(phenylmethyl)amino]carbonyl]propyl]amino]-1-(2-methylpropyl)-5-oxopentyl]-3-[methyl[(phenylmethyl)sulfonyl]amino]-5-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:55021 CAPLUS Full-text
DN 142:134323
TI Preparation of phenylcarboxylate esters as β-secretase inhibitors for the treatment of Alzheimer's disease

IN Nantermet, Philippe G.; Rajapakse, Hemaka Anthony; Selnick, Harold G.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005004803	A2	20050120	WO 2004-US20525	20040625
	WO 2005004803	A3	20050421		
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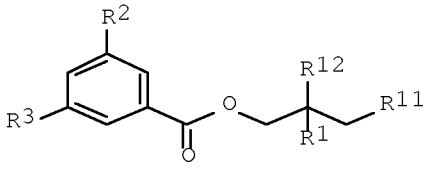
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004255191	A1	20050120	AU 2004-255191	20040625
	CA 2530006	A1	20050120	CA 2004-2530006	20040625
	EP 1643986	A2	20060412	EP 2004-756168	20040625
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	CN 1909897	A	20070207	CN 2004-80018651	20040625
	JP 2007522088	T	20070809	JP 2006-518686	20040625
	US 2006149092	A1	20060706	US 2005-562470	20051222
PRAI	US 2003-484150P	P	20030701		
	WO 2004-US20525	W	20040625		

OS MARPAT 142:134323
GI



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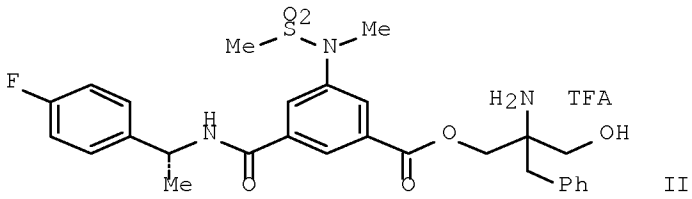


II

AB Title compds. [I; R1, R5, R9, R10 = H, (substituted) alkyl, alkenyl, alkynyl; R2 = R4SO2NR7, (substituted) Ph; R4 = (substituted) alkyl, alkenyl, alkynyl, Ph, PhCH2; R7 = H, alkyl, alkenyl, alkynyl; R3 = (substituted) PhCHR5NHCO, R9R10NHCO, etc.; R9R10 = atoms to form (substituted) pyrrolidinyl, piperidinyl; R11 = OH, alkoxy, phenylalkoxy, PhO, Ph; R12 = NR9R10, OH], were

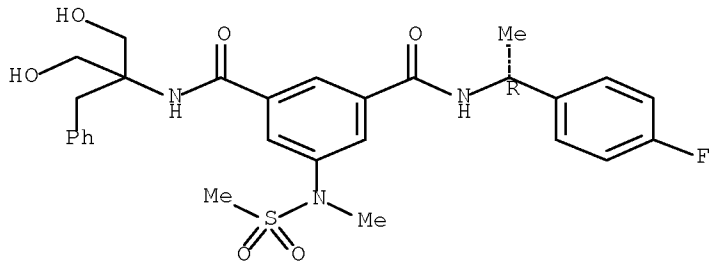
prepared as β-secretase inhibitors for the treatment of Alzheimer's disease (no data). Title compound (II) was prepared in several steps.

IT 827039-72-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenylcarboxylate esters as β-secretase inhibitors for the treatment of Alzheimer's disease)

RN 827039-72-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N1-[1,1-bis(hydroxymethyl)-2-phenylethyl]-N3-[(1R)-1-(4-fluorophenyl)ethyl]-5-[methyl(methylsulfonyl)amino]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:956793 CAPLUS Full-text

DN 142:16237

TI Structure-Based Design of Potent and Selective Cell-Permeable Inhibitors of Human β-Secretase (BACE-1)

AU Stachel, Shawn J.; Coburn, Craig A.; Steele, Thomas G.; Jones, Kristen G.; Loutzenhiser, Elizabeth F.; Gregro, Alison R.; Rajapakse, Hemaka A.; Lai, Ming-Tain; Crouthamel, Ming-Chih; Xu, Min; Tugusheva, Katherine; Lineberger, Janet E.; Pietrak, Beth L.; Espeseth, Amy S.; Shi, Xiao-Ping; Chen-Dodson, Elizabeth; Holloway, M. Katharine; Munshi, Sanjeev; Simon, Adam J.; Kuo, Lawrence; Vacca, Joseph P.

CS Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA

SO Journal of Medicinal Chemistry (2004), 47(26), 6447-6450
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

OS CASREACT 142:16237

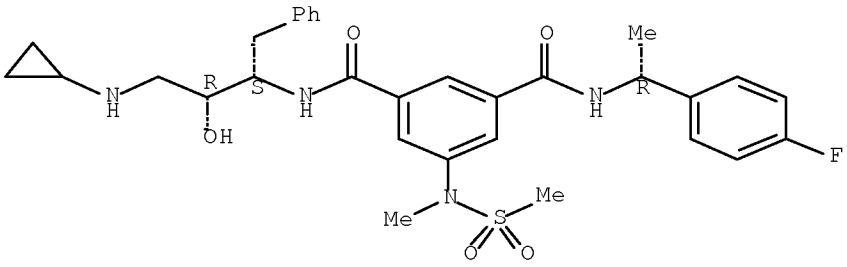
AB We describe the development of cell-permeable β-secretase inhibitors that demonstratively inhibit the production of the secreted amino terminal fragment of an artificial amyloid precursor protein in cell culture. In addition to potent inhibition in a cell-based assay (IC50 < 100 nM), these inhibitors display impressive selectivity against other biol. relevant aspartyl proteases.

IT 695216-22-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(structure-based design of potent and selective cell-permeable inhibitors of human β-secretase (BACE-1))

RN 695216-22-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N-[(1S,2R)-3-(cyclopropylamino)-2-hydroxy-1-(phenylmethyl)propyl]-N'-[(1R)-1-(4-fluorophenyl)ethyl]-5-[methyl(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:775885 CAPLUS Full-text
DN 141:295745
TI Preparation of hydroxyethylamine derivatives for the treatment of Alzheimer's disease
IN Demont, Emmanuel Hubert; Redshaw, Sally; Walter, Daryl Simon
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004080376	A2	20040923	WO 2004-EP2644	20040311
	WO 2004080376	A3	20041111		
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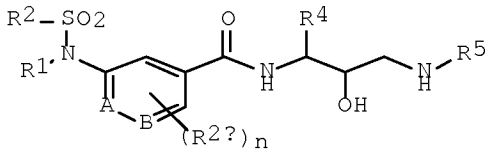
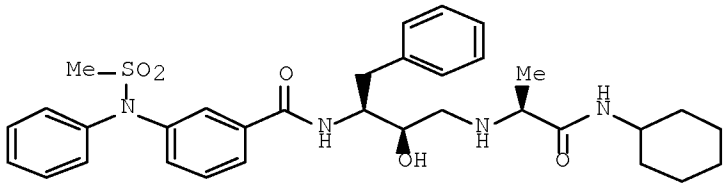
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1611089	A2	20060104	EP 2004-719453	20040311
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
	JP 2006520358	T	20060907	JP 2006-504685	20040311
	US 2006211740	A1	20060921	US 2005-549349	20050913
PRAI	GB 2003-5918	A	20030314		
	WO 2004-EP2644	W	20040311		

OS MARPAT 141:295745
GI



I



II

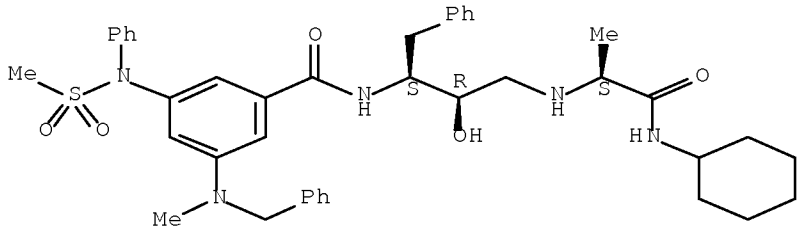
AB The invention relates to novel hydroxyethylamine compds. I [R1 is aryl or heteroaryl; R2 is alkyl or cycloalkyl; R2a is H, halo, alkyl or alkoxy; n is 0-2; A is -CR2b= or -N=, where R2b is H, alkyl, alkenyl, halo, alkoxy, amino, cyano or hydroxy; B is -CR3= or -N=, where R3 is H, halo, (un)substituted alkyl, aryl, carboxy, etc.; R4 is alkyl, cycloalkyl-, aryl-, heteroaryl- or heterocyclylalkyl; R5 is H, (un)substituted alkyl, aryl, -CRaRb-CONH-alkyl (Ra, Rb are H, alkyl or cycloalkyl), etc.] having Asp2 (β-secretase, BACE1 or Memapsin) inhibitory activity for use in the treatment of diseases characterized by elevated β-amyloid levels or β-amyloid deposits, particularly Alzheimer's disease. Thus, compound II was prepared by EDC/1-hydroxybenzotriazole-mediated coupling of 3-[(methanesulfonyl)phenylamino]benzoic acid with (S)-2-[(2R,3S)-3-amino-2-hydroxy-4-phenylbutylamino]-N-cyclohexylpropionamide dihydrogen chloride.

IT 761431-27-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of benzoic acid hydroxyethylamide derivs. for treatment of Alzheimer's disease)

RN 761431-27-0 CAPLUS

CN Benzamide, N-[(1S,2R)-3-[[(1S)-2-(cyclohexylamino)-1-methyl-2-oxoethyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-[methyl(phenylmethyl)amino]-5-[(methylsulfonyl)phenylamino]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 29 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:428903 CAPLUS Full-text
DN 141:6920
TI Preparation of phenylcarboxamide derivatives as β-secretase inhibitors for the treatment of Alzheimer's disease
IN Coburn, Craig A.; Stachel, Shawn J.; Vacca, Joseph P.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004043916	A1	20040527	WO 2003-US35316	20031106
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2505098	A1	20040527	CA 2003-2505098	20031106
	AU 2003291308	A1	20040603	AU 2003-291308	20031106
	EP 1562897	A1	20050817	EP 2003-768700	20031106
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2006514623	T	20060511	JP 2004-551780	20031106
	US 2006052615	A1	20060309	US 2005-534291	20050509
	US 7109217	B2	20060919		
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	US 2002-425560P	P	20021112		
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	US 2005-534291	A3	20050509		

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

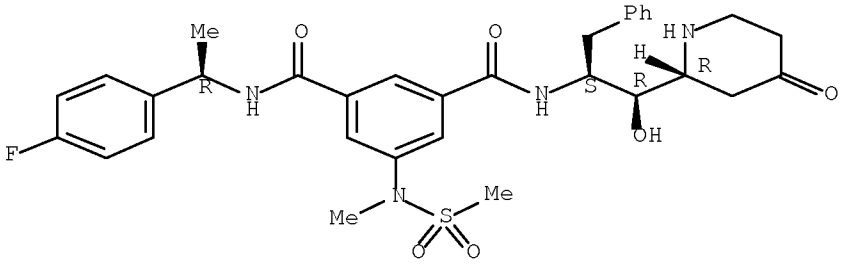
AB The title compds. I [R2 = R4-S(O)m-NR5-, R4-S(O)m-, R4NHCO-, R4CONH-, R4R5N-, CN, halo, etc.; R4, R5 = H, C1-C6alkyl, Ph or benzyl; R6a, R6b, R6c = H, halo, -OR5, -SR5 or C1-C6alkyl; X1 = H; X2 = OH, or X1, X2 = oxo; Z = CO, CH-OH, CH-F, or ethylene ketal; n = 1-4; m = 0-2] were prepared as β-secretase inhibitors for the treatment or prevention of diseases, such as Alzheimer's disease. For example, compound II was prepared from di-Me 5-aminoisophthalate in a multi-step synthesis. The compds. of the invention exhibited inhibiting activity against β-secretase with an IC50 from about 1nM to 1 μM.
IT 695215-64-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of phenylcarboxamide derivs. as β-secretase inhibitors for the treatment of Alzheimer's disease)

RN 695215-64-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N-[(1R)-1-(4-fluorophenyl)ethyl]-N'-[(1S,2R)-2-hydroxy-2-[(2R)-4-oxo-2-piperidinyl]-1-(phenylmethyl)ethyl]-5-[methyl(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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